Vol. 12 OCTOBER, 1936 No. 4

THE AMERICAN HEART JOURNAL

A JOURNAL FOR THE STUDY OF THE CIRCULATION

PUBLISHED MONTHLY
UNDER THE EDITORIAL DIRECTION OF
THE AMERICAN HEART ASSOCIATION

PUBLISHED BY THE C. V. MOSBY COMPANY, 3523-25 PINE BLVD., ST. LOUIS, U. S. A.

The American Heart Journal

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Vol. 12, No. 4, October, 1936. American Heart Journal is published monthly by The C. V. Mosby Company, 3523 Pine Blvd., St. Louis, Mo. Subscription Price: United States, its Possessions, Pan-American Countries, Canada, $8.50 a year; Foreign, $9.50. Entered as Second-Class Matter at Post Office at St. Louis, Mo., under Act of March 3, 1879.

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Original Communications

THOROTRAST ARTERIOGRAPHY OF THE EXTREMITIES WITH REPORT OF ILLUSTRATIVE AND UNUSUAL CASES*

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WITH the use of stabilized thorium dioxide sol, arteriography has become a practical and apparently harmless diagnostic procedure and a valuable method for studying the circulation in the extremities. Although arteriography has been practiced in a small way for many years, it has been less than ten years since it began to gain popularity. Thorotrast has been employed by those who have had the greatest experience with this procedure. Abroad, those who have practiced the method in the extremities most extensively are dos Santos and his coworkers,[1, 2] Heuser[3] and Frieh and his associates, including Leriche.[4, 5] In this country the main workers in this field are Allen and Camp,[6] Veal and McFetridge,[7] Horton,[8] and Barker.[9] Besides being used for demonstrating roentgenographically the arteries of the extremities, thorotrast is used similarly by some for making arteriograms of the cerebral vessels and of the abdominal aorta. Edwards[11] and Allen[10] have reviewed the earlier work concerning arteriography. The veins are also well demonstrated by direct injection cephalad into the venous channels.

Thorotrast,† a stabilized 25 per cent (by volume) colloidal solution of thorium dioxide, was first used in man in 1929 by Paul Radt,[12] formerly of Berlin, for demonstrating radiologically the liver and spleen. Thorium dioxide, being radiopaque and of high molecular weight, is rapidly removed from the blood stream and engulfed by the reticuloendothelial cells of the body, and, where these are most concentrated, casts a shadow on the x-ray plate. As much as 75 c.c. is used for hepatosplenography. Because of a small degree of radioactivity, very

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Read before the American Heart Association, Section for the Study of Peripheral Circulation, at Kansas City, Mo., May 12, 1936.

†Manufactured by the Heyden Chemical Corporation of New York.

slow elimination and possible latent increase in the degree of radioactivity, the Council on Pharmacy and Chemistry of the American Medical Association has not accepted thorotrast as an approved chemical for use in man. Unfortunately, Radt, who has had the longest experience with it, has left Berlin and has lost access to his records and the follow-up of his patients. However, Rigler and his coworkers,[13] in employing thoratrast for hepatosplenography in 175 patients over a period of three and a half years, did not observe immediate or remote ill effects. Yater, Otell, and Hussey,[14] using this preparation in total doses of 75 c.c. for the same purpose in more than 200 patients over a period of nearly five years, have likewise not observed harmful effects.

The amount of thorotrast used for arteriography is much less than that used for hepatosplenography, unless several examinations are made, and any possible danger is therefore considerably lessened. For the upper extremity 5 to 12 c.c. (average 8 c.c.) are usually sufficient to produce good films. For the lower extremity 10 to 12 c.c. are commonly employed. Those who have practiced arteriography most have not noted ill effects. It is fair to mention, however, that several French authors have reported injury attributed to the procedure.

Because thorotrast when injected into the blood stream rapidly leaves the vascular system, films must be taken almost immediately to demonstrate the arterial tree, whereas for hepatosplenography the films may be made any time after several hours following the last injection.

TECHNIC OF ARTERIOGRAPHY OF THE EXTREMITIES

A routine technic has been used in our institution which for practical purposes gives satisfaction. Two films are usually sufficient for the upper extremity, two or three films for the lower extremity. In the upper extremity the injection is made through the skin into the brachial artery in the antecubital space just medial to the lacertus fibrosus, the needle pointing toward the axilla. In the lower extremity the injection is made through the skin into the common femoral artery 2 to 3 inches below the inguinal ligament, with the needle pointing toward the pelvis. The first two fingers of the left hand palpate the artery proximal to the point of injection and hold it in position. The needle, with the bevel up, is slowly inserted into the lumen of the artery for 1 to 2 cm. as nearly parallel with the artery as possible. When the needle is within the lumen of the artery, bright red blood spurts into the syringe with each beat of the heart, forcing the piston steadily outward. When this happens, the vessels well above the needle are occluded, and the thorotrast is injected with moderate rapidity but not hastily. If the injection requires more than moderate pressure or is attended with pain the needle is either plugged by a clot or a piece of tissue, or is not in proper position but is either in the wall of the artery or in the surrounding tissues. The occlusion of the needle should then be removed and the needle reinserted. After some experience the procedure is fairly simple. However, if there is much difficulty encountered in puncturing the artery because of deep position of the vessel, excessive fat, subcutaneous hemorrhage or edema, or spasm of the artery, it is perhaps wiser to desist or at least to postpone the attempt. An 18 gauge, 2 inch long, preferably new needle is most useful for the injection. Arteriography, of course, must be performed aseptically.

To prevent spasm of the punctured artery and to relieve the patient's apprehension, I regularly inject intravenously 1 ampule of spasmalgin* about fifteen minutes before the procedure.

The patient lies supine on the x-ray table, and the x-ray plate is placed under the extremity to be studied. Films measuring 14 by 17 inches are used except for the foot alone. Two exposures are made on each film, one-half of the film being covered by a lead shield while the other half covered by the limb is being exposed. After the region of the extremity to be used for injection is prepared and draped with sterile towels, the skin and tissues around the artery are anesthetized with a local anesthetic, such as 1 per cent novocaine. When the arm is to be filmed, a sphygmomanometer cuff previously applied is pumped up above the systolic pressure after the artery has been punctured. Approximately 8 c.c. of thorotrast (which is marketed in ampules of 12 c.c. and 25 c.c.) is then injected, the thorotrast being at room temperature and undiluted. As soon as the injection is completed, the needle is withdrawn, and pressure with an alcohol sponge made at the point of injection to prevent leakage of blood from the artery. The forearm and hand, palm upward and digits slightly separated, are rapidly posed on the plate. The first exposure is then made. The arm and hand are next shifted to the other half of the film and posed, and the lead shield is placed on the exposed half. The sphygmomanometer cuff is then rapidly deflated and four beats allowed to pass into the forearm, when the second exposure is made. These two films usually show the arteries of the forearm well filled. In the first film usually the palmar arch is also shown, and in the second film some of the digital arteries are frequently demonstrable. In the latter film some of the veins are also often filled.

When the lower extremity is to be filmed, half of the plate is placed so that the lower two-thirds of the thigh and the upper fourth of the leg in the anteroposterior position is on half of the film. After the injection of approximately 12 c.c. of thorotrast has been made into the femoral artery, an assistant gently occludes the artery against the pubic bone with his fingers. The first exposure is then made. With the artery still occluded, the plate is shifted downward so that the rest of the extremity, either in the anteroposterior position or slightly flexed in the lateral position, is on the unexposed portion of the film. The fingers of the assistant are removed from the artery for five heartbeats and reapplied, the second exposure then being made. If a third film showing the foot placed sole downward is desired, the leg is flexed at the hip and knee and the foot is posed on a smaller plate. The assistant then removes his fingers, and the exposure is made. The first film shows the large arteries of the thigh and the branching of the popliteal artery. The second film shows the main arteries of the leg and foot. The third film often shows the main arteries of the foot but rarely much of the digital branches.

The following x-ray technic is employed: Tube distance 30 inches, 0.5 mm. aluminum filter, high speed screens, 100 milliamperes, 2/10 second, voltage varied according to thickness of the part (3 cm., 46 K.V.P.; 4 cm., 47 K.V.P.; 5 cm., 49 K.V.P.; 6 cm., 52 K.V.P.; 7 cm., 55 K.V.P.; 8 cm., 57 K.V.P.; 9 cm., 59 K.V.P.; 10 cm., 62 K.V.P.; 11 cm., 65 K.V.P.; 12 cm., 68 K.V.P.; 13 cm., 71 K.V.P.; 14 cm., 74 K.V.P.; 15 cm., 76 K.V.P.).

This technic, after some experience, usually gives all of the information desired. It can be used in any hospital without special equipment. A more ideal method is that of Caldas[15] with his radio carousel, a costly apparatus which permits six exposures of the same part to be made at intervals of one second after the injection of the contrast medium. This method, while ideal in many respects, is not absolutely necessary, but it gives more exact information as to the rate of circulation in the extremity, and it obviates the necessity of timing.

*Spasmalgin, prepared by Hoffmann-LaRoche, Inc., contains in each ampule of 1 c.c., papaverine hydrochloride 0.02 gm. (1/3 grain), pantopon 0.01 gm. (1/6 grain), and atrinal (atropine sulphuric acid ester) 0.001 gm. (1/60 grain).

CAUTIONS IN INTERPRETATION

Great caution must be observed in interpreting films in which there is incomplete filling of the vessels. If there is doubt as regards the possibility of obstruction, the arteriograms should be made again and a little more time given for the contrast medium to fill the arteries in question. Normally it takes "from six to nine seconds for the column of thorotrast, after it enters the blood stream, to pass from the femoral triangle down to the vessels of the foot, the return flow, naturally, being slower" (Veal and McFetridge). Vascular disease, of course, causes variations in the rate of progression of the column, as does also any increase or decrease in the rate of the systemic circulation.

Filling of the digital vessels of the hand and even more so of the foot is the most uncertain feature of the procedure. Even in normal limbs when several of the digital arteries are filled, the others may not be. Fortunately, most of the data usually desired concern the larger vessels of the extremity.

REACTIONS

Systemic reactions of any consequence due to the injection of thorotrast are rarely encountered. However, if some of the medium is injected into the tissues about the artery there is usually severe local pain with some local swelling and heat. In hypersensitive individuals the pain may be felt in the whole extremity. Hot moist compresses and analgesic drugs give considerable relief, and the effects subside in from two to four days. Even if the thorotrast is injected into the wall of the artery, no serious damage is done.

THE NORMAL ARTERIOGRAM AND THE COLLATERAL CIRCULATION

A knowledge of the normal arteriogram is essential in interpreting abnormal states. This may be obtained by dissection of cadavers and amputated extremities, by the study of arteriograms of normal extremities, and by the study of arteriograms of the injected cadaver or of amputated limbs. Although there are many variations of the normal vascular tree of the extremities, the main arteries usually conform to a standard pattern.

Radiograms of normal limbs of cadavers injected with a radiopaque substance show a voluminous vascular tree; whereas, arteriograms of living subjects with normal extremities show relatively few vessels, mainly the larger ones and comparatively few of their cutaneous, muscular, osseous and anastomotic branches, especially in the lower extremity. The former is explained by the fact that there is no circulation in dead limbs and all vessels washed out and refilled with the contrast medium are demonstrated. In the resting extremity of the normal living subject, however, only those vessels contain the thorotrast which

are just sufficient to nourish the tissues in a state of relative inactivity. Furthermore, owing to the circulation of blood and a lag in the diffusion of the thorotrast, only a certain number of vessels are made visible at

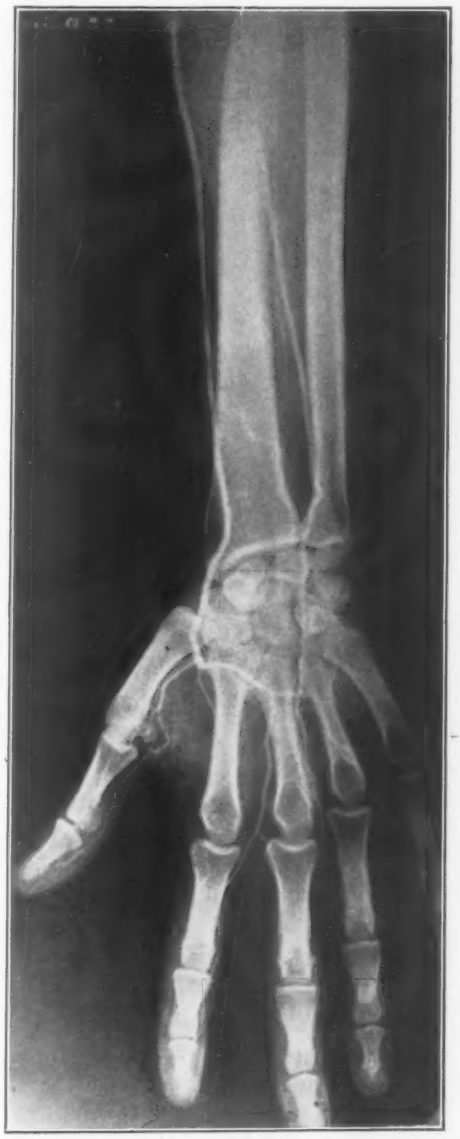

Fig. 1.—Normal arteriogram of forearm and hand.

any one instant. If arteriograms could be made while the subject were running, undoubtedly a great many more vessels would be seen to contain the contrast medium since the muscular branches would be functioning more effectively and the diffusion would be more rapid.

The normal arteriogram shows the arteries to be smooth walled, relatively direct in their course, and very gradually tapering down to the smallest branches (Fig. 1). When visible, the veins are seen to be of greater lumen, not so opaque, and much more wavy, tortuous and interlacing. The sites of the valves in the larger veins are often discernible, due mainly to localized bulging just above them.

When there is obstruction of an artery from any cause, the so-called collateral circulation becomes apparent. The head of pressure being the same as before the obstruction took place, more blood is forced down the branches arising from the occluded vessel proximal to the point of occlusion. The number of collateral vessels made visible depends upon the degree of involvement of the branches of the obstructed artery or arteries, the rapidity of the occlusion, and the state of the general circulation. Allen[16] and others are probably correct in assuming that most, if not all, of the so-called collateral vessels are vessels which previously existed, since a comparison with the radiograms of the injected normal limbs of cadavers shows in general the same vessels, since the collateral vessels are demonstrable relatively soon after the occlusion occurs, and since the main collateral vessels are relatively large and lengthy. However, it is quite possible that new anastomoses may develop in time since vessels are seen in cases of gradual occlusion passing from the artery above the area of occlusion or from another vessel to join the occluded vessel below the area of occlusion and thus bridging the gap (Fig. 2). Most of the collateral vessels are either normal anastomotic branches or muscular branches. In time they become larger in diameter of lumen, stretched and elongated, and often tortuous and resembling a corkscrew. Many of their smaller branches may arise more or less at a right angle. Many more small and apparently interlacing vessels are also demonstrable in the arteriograms after occlusion of an artery.

The fact that the normal arteriogram shows relatively few vessels and mainly the larger and more direct ones probably explains why it is usually the larger arteries that are most affected by degeneration. These are the vessels bearing the brunt of the circulatory load, and the factor of strain is important in the localization of degenerative processes. The smaller, less constantly used vessels are frequently less severely affected and are able therefore in many cases to come to the aid of the damaged limb and to take over part or all of the function of the affected vessel.

ARTERIOSCLEROTIC GANGRENE AND SELECTION OF THE SITE OF AMPUTATION

Although arteriography is of interest and probably of value in studying the pathologic-physiologic disturbances of the circulation in the extremities, undoubtedly its greatest practical value lies in its use for helping to determine the best site for amputation of the lower extremity in cases of arteriosclerotic gangrene. Veal and McFetridge[7] have

stressed the value of arteriography for this purpose. However, it by no means dispenses with the other forms of clinical examination.

Arteriosclerosis is manifested by irregularity in the wall of the artery and narrowing or obliteration of the lumen at intervals. The larger

Fig. 2.—Arteriosclerosis obliterans. Anterior tibial artery interrupted in lower half, posterior tibial in upper half. Small collateral arteries bridging across the gaps. Collateral arteries numerous in the calf.

arteries are often wavy instead of straight. Small branches may end abruptly. This process affects mainly the larger arteries but often also the medium-sized and even the small ones. In uncomplicated arterio-

sclerosis the number of smaller arteries, or collaterals, is often moderately or greatly increased, depending upon the degree of involvement of the larger arteries and the relatively mild or moderate involvement of the muscular and other branches. In other words, the greater the involvement of the large arteries and the less the involvement of the smaller arteries, the more extensive the collateral circulation will be.

Although gangrene may be due to simple diminution in caliber of the lumen, it is more often due to thrombosis of one of the larger

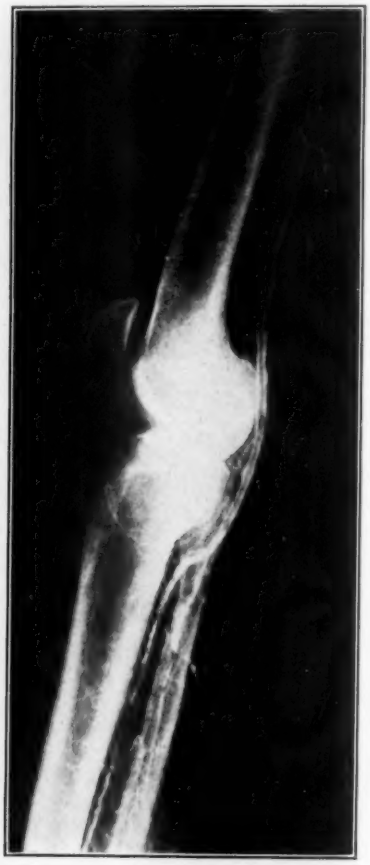

Fig. 3.—Arteriosclerosis obliterans. Occlusion of posterior tibial artery. Gangrene of foot.

degenerated arteries. When the gangrene is due to simple occlusion of the lumen by the arterial degeneration, usually only a toe or two is affected, whereas, when there is more extensive gangrene, thrombosis and occasionally embolism may be assumed to exist. The thrombus usually extends well above the upper limit of gangrene.

For instance, a diabetic patient aged seventy-two years developed gangrene of the toes of the left foot. The arteriogram (Fig. 3) showed complete occlusion of the posterior tibial artery about 5 cm. below its origin, as well as severe arterio-

sclerosis of the other arteries. Amputation was performed in the middle of the thigh, but even then there was some sloughing of the stump, requiring a secondary operation.

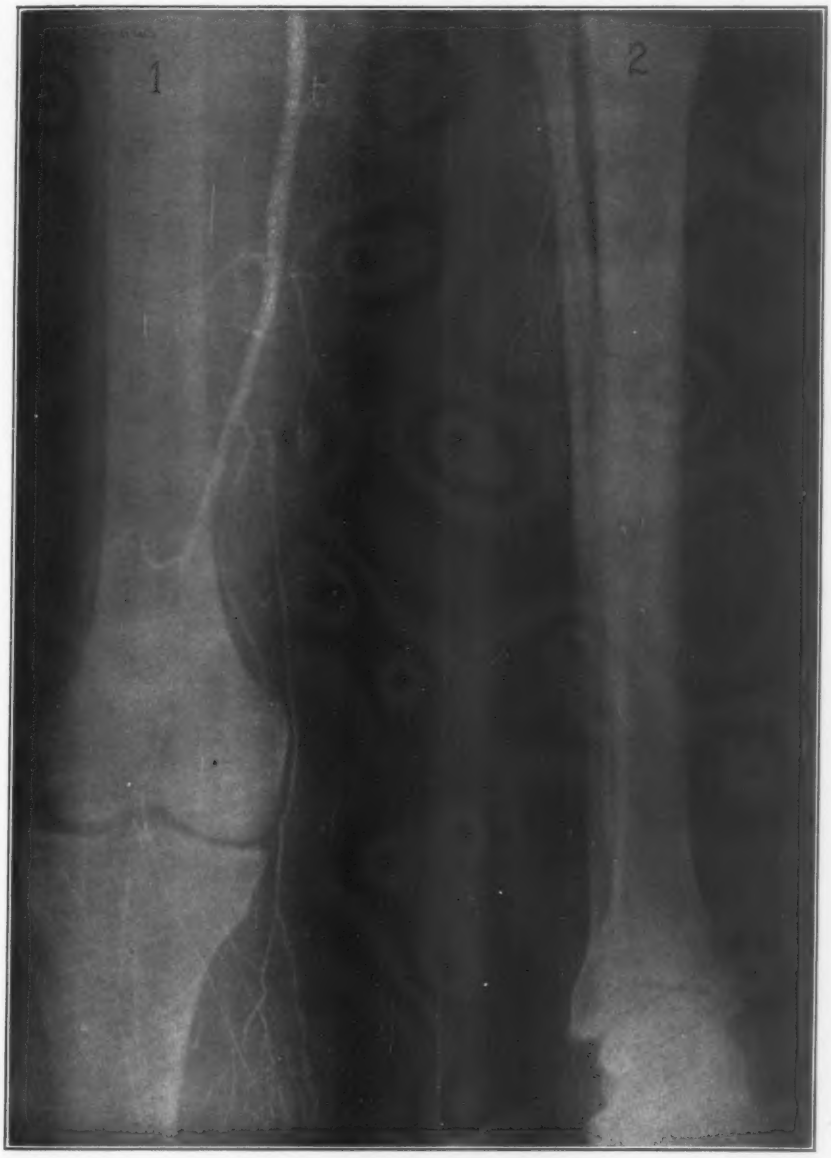

Fig. 4.—Thromboarteriosclerosis obliterans. Complete occlusion of popliteal artery by a thrombus. Large, dry ulcer on heel. Practically no arteries visible below calf.

Another diabetic, aged fifty-seven years, developed an indolent shallow ulcer on the heel of the right foot with edema of both legs. Although thermographic and oscillometric studies revealed that the occlusion was above the knee, the arterio-

gram (Fig. 4) showed definitely that there was complete occlusion in the upper portion of the popliteal artery with relatively little collateral circulation even after two months. Amputation was performed in the lower third of the thigh. Dissection and study of the vessels showed an old thrombus beginning 3.5 cm. below the site of amputation, extending for 10.5 cm. and ending 2.5 cm. above the origin of the anterior tibial artery. All of the larger arteries were markedly arteriosclerotic and calcified. There were other thrombi and sites of simple occlusion in the main branches of the popliteal artery. Most of the veins were also thrombosed. Healing was uneventful.

In still another patient, a negress, aged forty-five years, with advanced carcinoma of the uterus, a severe pain had suddenly developed in the calf of the right leg two weeks before admission to the hospital. The pain continued, and the

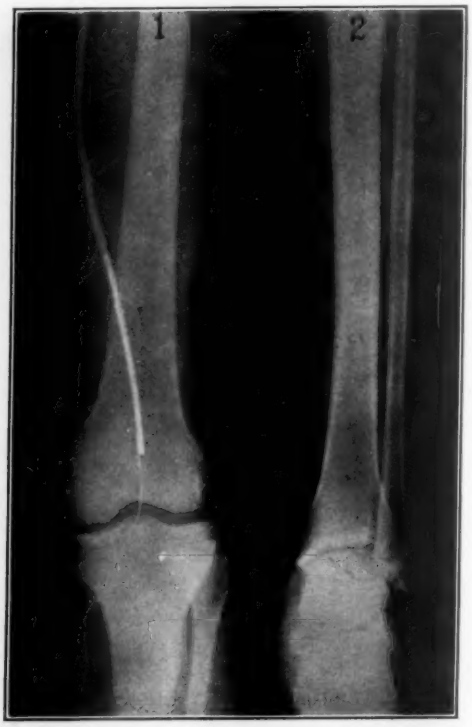

Fig. 5.—Embolic occlusion of popliteal artery. Gangrene of foot and lower third of leg. Very few collateral arteries visible below knee.

leg began to swell. The foot became cold and insensitive. The whole foot and lower third of the leg were found to be cold, smooth and dry, and the toes were becoming shriveled. Pulsations in the dorsalis pedis and posterior tibial arteries could not be felt, but it was thought that pulsation could be obtained in the popliteal artery. However, an arteriogram showed abrupt occlusion of the popliteal artery (Fig. 5) just above the knee joint, and relatively little collateral circulation below the knee. Amputation was performed at the knee joint. Dissection and study of the vessels of the amputated limb showed a gray thrombus, apparently an embolus, in the popliteal artery beginning 8 cm. below the site of amputation and extending far down into the two tibial and the peroneal arteries. There was moderately severe atherosclerosis. The veins were distended and filled with relatively fresh thrombi. Healing was complicated by secondary infection of the stump.

THROMBOANGIITIS OBLITERANS (BUERGER'S DISEASE)

Arteriography in cases of thromboangiitis obliterans, while of questionable practical value, is nevertheless of great importance in the study of the pathogenesis of the disease. It shows definitely that the disease

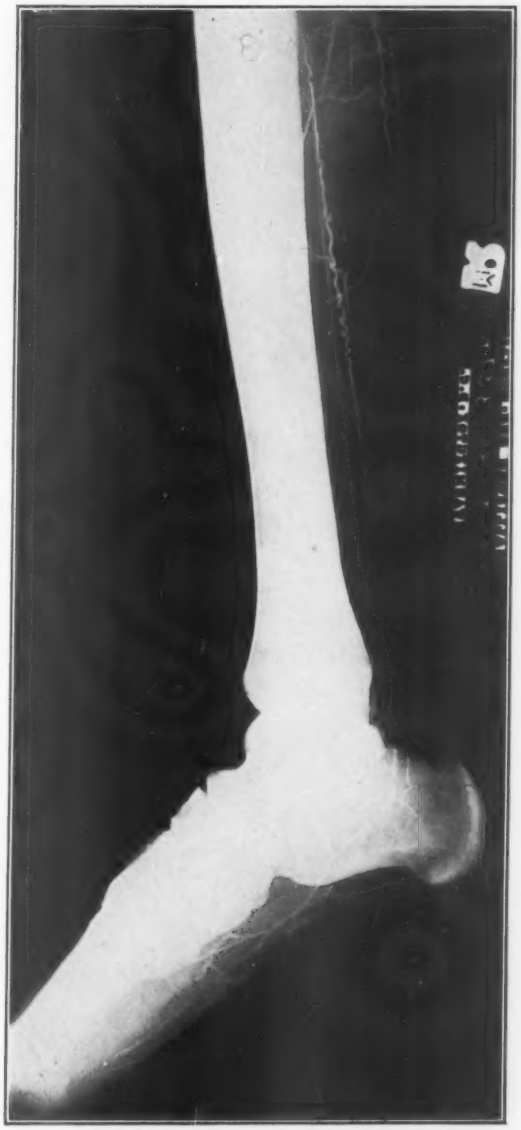

Fig. 6.—Thromboangiitis obliterans. Main vessels almost entirely occluded. Long, wavy collateral arteries nourishing leg. Lesions healed.

frequently involves all four extremities. It shows also that it is a polyphasic disease, i.e., various stages of the disease may be present in various arteries and branches in the same limb. The collateral circulation is the most extensive of all vascular diseases, but even the

collaterals may become involved. Brief accounts of a few cases will serve to illustrate some of the main characteristics of the disease.

In the case of an Irishman, aged thirty-two years, who had had manifestations of Buerger's disease of the legs for only a year, gangrene of the left foot pro-

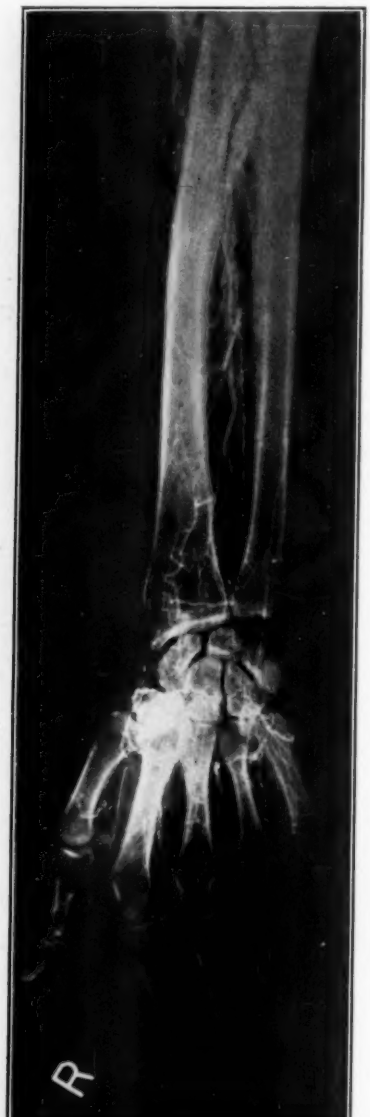

Fig. 7.—Thromboangiitis obliterans. Radial and ulnar arteries practically completely occluded. Small collateral arteries and extension of interosseous supply hand. No trophic changes in hand.

gressed rapidly during a severe attack of pharyngeal diphtheria, while the pregangrenous condition of the right foot improved. Amputation was performed above the left knee, followed by fairly rapid healing of the stump. Although the right foot at the time showed very little trophic change, arteriograms revealed that

all of the large vessels below the knee were practically completely occluded and that the circulation was maintained by long wavy collateral arteries (Fig. 6). There was clinical evidence that the ulnar arteries might be involved, although the circulation in the hands appeared to be normal. Arteriograms of the left forearm and hand showed that the lower end of the ulnar artery from just above the wrist joint was obliterated, but a small collateral branch continued down from the upper end of the occluded portion and joined the palmar arch. The interosseous artery also sent branches down into the palm. The other arteries appeared to be normal. This patient later died of a cerebral abscess complicating a pulmonary abscess, and dissection and study of the vessels of the leg showed extensive involvement of all of the main arteries and some of the veins, including the femoral.

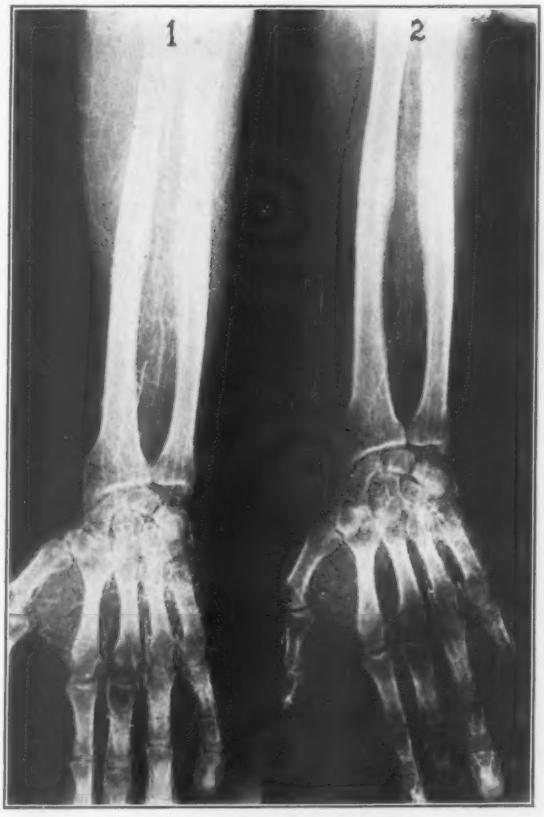

Fig. 8.—Thromboangiitis obliterans. Extensive and extreme involvement of radial, ulnar, and interosseous arteries. Many fine collaterals supply blood to forearm and hand. Tip of second finger had been lost and bed of thumb nail was infected.

Another Gentile, aged forty-seven years, who had had his right leg amputated above the knee eleven years before and who lately had been having severe pain in the left foot with evidence of impending gangrene, had absence of pulsation in the radial and ulnar arteries of both hands, although the circulation was quite adequate. Pulsations could be felt in both interosseous arteries. Arteriograms of the right forearm and hand showed both the radial and ulnar arteries to be completely occluded in their entire extent (Fig. 7). Long, twisting collateral arteries passed down into the hand and together with prolongation of branches of the interosseous artery maintained a good blood supply to the hand and fingers.

A Jew, aged thirty-eight years, had had a typical history of thromboangiitis obliterans for six years. Some toes had been lost by spontaneous and surgical amputation, and the distal phalanx of the right index finger had also amputated itself.

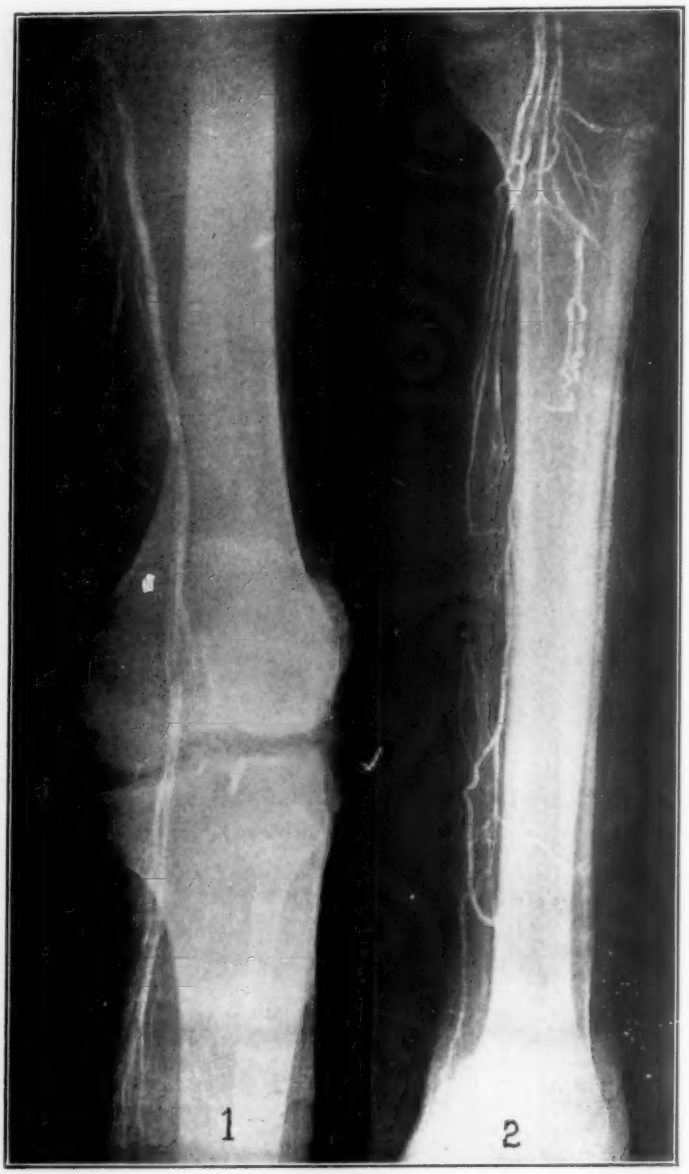

Fig. 9.—Thromboangiitis obliterans. Same case as Fig. 8. Popliteal and tibial arteries occluded. Main blood supply to leg and foot by way of sural branches. Gangrene of toes.

While he was in the hospital recently because of severe gangrene of both feet, precipitated by frost-bite, arteriograms were made of the arms and legs. The vessels of the left arm and hand were essentially normal, but the radial, ulnar,

and even the interosseous arteries of the right were almost completely occluded, and the circulation was maintained by a great number of thin, interlacing collaterals (Fig. 8). This is the first case I have seen with severe involvement of the interosseous artery from any cause. The arteriograms of the lower limbs presented essentially the same appearance. The popliteal artery and its main branches were completely occluded from just below the knee joint. Practically all of the blood supply to the leg and foot was obtained by extensions and ramifications of the sural arteries, the two large inferior muscular branches of the popliteal artery which are normally distributed to the gastrocnemius, soleus and plantaris muscles (Fig. 9).

An arteriogram of the arm and hand of a Gentile aged thirty-eight years, who eight years before had had lumbar sympathetic ganglionectomy and ramisectomy followed by remission of all pregangrenous manifestations, was normal; but during injection of the thorotrast into the brachial artery he suffered excruciating pain in the forearm and hand, followed by absence of arterial pulsations and blanching of the hand for several minutes.

This is the second case I have seen of severe arterial spasm due to arterial puncture in spite of the previous administration of papaverine. It indicated in this case that there was a large element of spasm associated with the thromboangiitis obliterans and explained the success of the ganglionectomy and ramisectomy. There was no question of the diagnosis of thromboangiitis obliterans, since attacks of superficial phlebitis had occurred and other evidences of the disease existed. Intravenous injection of a second ampule of spasmalgin quickly relieved the spasm, but pain at the site of injection continued for some time, apparently due to the injection of a small amount of thorotrast into the tissues. The other case of arterial spasm concerned a woman with Raynaud's disease, whose artery I tried to inject while she was having an attack.

ARTERIOVENOUS FISTULA

Both congenital and acquired arteriovenous fistulas are demonstrable by arteriography. Besides showing the exact site or sites of fistulas the arteriograms indicate the size of the fistula but not the extent of the collateral circulation. Horton and Ghormley[17] and Frieh and Lévy[18] have had experience with congenital fistulas. I have made arteriograms in four cases of the acquired form, one of which was reported in 1933 by Yater and White.[19]

Horton and Ghormley[17] have pointed out that in congenital arteriovenous fistula there are increased size and tortuosity of arteries leading to the fistula, "pooling of the medium in the region of the fistula, and absence of filling of the arteries distal to the fistula."

In acquired fistulas the appearance of the arteriograms is dependent mainly upon the size of the fistula and the size of the vessels involved. Usually the fistula involves a relatively large artery and vein, since it is most often produced by gunshot or stab wounds and the missile must pass through both the artery and vein without completely severing them. The small fistulas are usually due to buckshot.

When the fistula is small and single, the arteries both above and below the fistula may be seen in the arteriogram; when large, they are probably never seen, the reason being that in the latter practically all of the blood passes rapidly from the artery through the fistula into the veins. In a small fistula the veins distal to the fistula are not so large, numerous or tortuous as they are in the case of a large fistula. In either case there is a saccular enlargement of the vein in the region of the fistula, its size being dependent also on the size of the fistula and the size of the vessels involved. This is not a true aneurysmal sac, but merely a dynamic enlargement which collapses after death or removal at operation.

With large fistulas the veins distal to the communication assume the rôle of the arteries in nourishing the extremity. This arrangement might work satisfactorily if it were not for the difficulty in the return of venous blood from the part. As a matter of fact, just how it gets back to the veins proximal to the fistula is unknown, but the study of one of my cases suggested a mechanism.

A brief report of the four cases studied will demonstrate these features. A more detailed report of the cases will be published elsewhere.

The first case was that of a negro boy, aged fifteen years, who had been shot with buckshot, five months before, in the right arm. All of the physical signs of arteriovenous fistula were present in the antecubital fossa. The arteriogram showed a saccular enlargement in the first part of the ulnar vein. The arteries distal to the sac were fairly well filled, as was also the brachial vein proximal to it but not the veins distally. These findings and the fact that there was little change in the pulse rate and blood pressure when the fistula was closed indicated that the fistula was very small.

The second case concerned a negro, aged forty-four years, who had been shot with a shotgun in the right popliteal region twenty-eight years before. His complaint was not related to the arteriovenous fistula, typical evidences of which were found in the right lower extremity. Arteriograms showed great enlargement of the femoral and great saphenous veins proximal to the fistula, with a saccular bulging behind the knee. The popliteal artery was not visible above or below the knee, but few of the veins below the sac contained the contrast medium. Operation revealed a very small fistula, and the sac was not apparent in the specimen.

The third case was that of a white man, aged thirty-four years, who had symptoms suggestive of subacute bacterial endocarditis. He had received a gunshot wound of the left thigh twenty-six years before. Physical signs of an arteriovenous fistula were prominent in Scarpa's triangle. In making the arteriogram the femoral artery had necessarily to be punctured just proximal to the fistula. The artery leading to the fistula was not demonstrable in the film. The vein formed a large fusiform sac in the upper thigh; the veins distal to it were visible but not distended or tortuous; and the artery was not evident. The fistula was thought to be of relatively small size. Operation, performed with the hope that bacterial vegetations might be present in the fistula, showed it to be about 2 mm. in diameter. No vegetations were found, as in the case of Hammon and Rienhoff,[20] and ten days later necropsy revealed subacute bacterial endocarditis.

In the fourth case, a negro, aged fifty-two years, had been shot through the left knee with a 0.38 caliber rifle fourteen years before. The leg was very large, and the superficial veins were very prominent. A large chronic ulcer was present on the an-

terior surface between the knee and the ankle. Six arteriograms made serially after the injection of 50 c.c. of thorotrast (the large amount being given because of the great size of the veins) did not show any of the main arteries, but the great

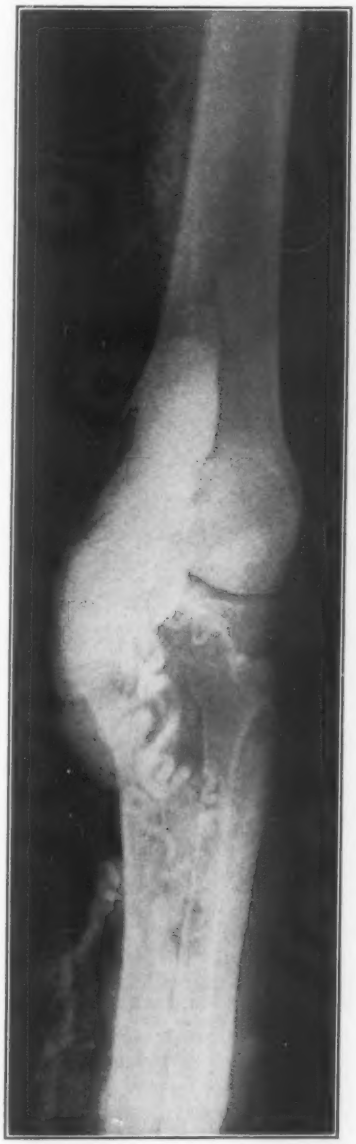

Fig. 10.—Large arteriovenous fistula between popliteal artery and vein. Film No. 2 of a series. Popliteal vein greatly dilated. Tributary veins numerous and tortuous. No arteries visible.

saphenous vein proximal to the fistula was well filled, and the popliteal vein was tremendously distended (Fig. 10). Subsequent films showed many very tortuous veins becoming visible below the fistula, while the saphenous and popliteal veins were not so distinct. In the last films, however, the distal veins became less distinct,

whereas the great saphenous and popliteal veins became visible again. These findings indicated that the fistula was a large one. They suggested also that the contrast medium went down the veins and came back the same way, there being apparently two simultaneous currents in the same vein.

ANEURYSM

Aneurysms are well demonstrated by arteriography, as shown by Frieh and Lévy.[21] Barker[9] has reported a case of spontaneous false aneurysm

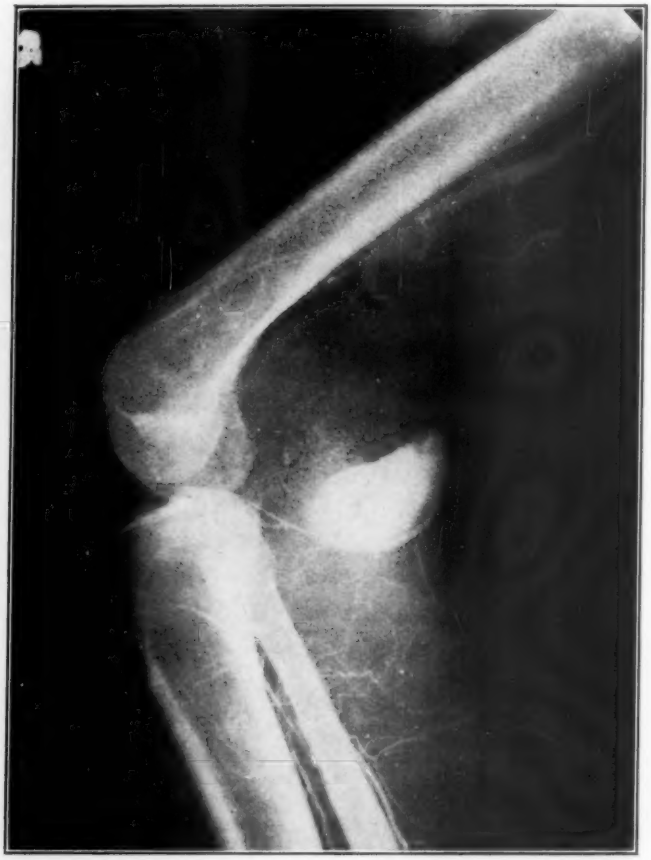

Fig. 11.—Ruptured popliteal aneurysm. Popliteal artery interrupted, but tibial arteries visible. Pool of thorotrast in upper calf.

of the popliteal artery so demonstrated. My series includes a case of ruptured popliteal aneurysm.

The patient was a negro, aged forty-nine years, who six months before had been struck in the calf of the right leg by a falling tub. This incident had been followed by swelling in this region, and when examined the whole leg was found to be greatly enlarged, with a soft mass in the popliteal fossa. On one occasion the femoral artery was injected with thorotrast, on another, the femoral vein. The first films showed interruption of the popliteal artery for some distance, with a pool

of thorotrast in the upper part of the calf (Fig. 11). The second films showed the popliteal vein compressed on the peripheral side of the swelling containing this pool, thus accounting for the edema. Dissection of the leg following amputation above the knee showed a very large hematoma in the calf, which had formed as the result of rupture of a small popliteal aneurysm, probably syphilitic.

UNUSUAL CONDITIONS

Arterial Spasm Due to Ergotamine Tartrate Resulting in Gangrene of the Feet.—Arteriograms were made in the case of a white fisherman, aged sixty-four years, who was given large doses of gynergen hypodermically to relieve pruritus due to the jaundice of toxic hepatitis. Evidence of impairment of circulation in

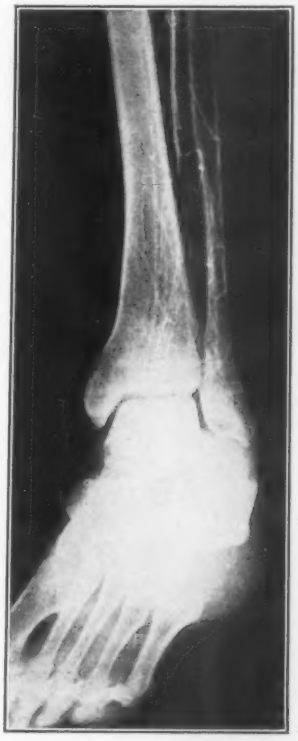

Fig. 12.—Spasm of tibial arteries due to overdosage of ergotamine tartrate. Occlusion in lower third of leg. Long collaterals to foot. Gangrene of distal halves of both feet.

both feet developed on the third day, and dry gangrene resulted after a few days. The arteriograms made more than a month later showed normal arterial shadows down to the lower third of the leg, where they faded out into a point (Fig. 12); long, thin collateral arteries passed downward to the foot from above the upper limits of occlusion. After amputation the arteries were found to be severely constricted and at intervals contained thrombi.

Thromboangiitis Obliterans (?) in a Negro.—A negro, aged forty-three years, had been having parts of the toes of both feet ulcerate and fall off for nine years. Pulsations were absent in both dorsalis pedis arteries and in the left posterior tibial artery. Arteriograms of the right leg showed the anterior tibial artery missing, the posterior tibial normal, and numerous collateral arteries in the leg and foot (Fig.

13). Arteriograms of the left leg showed obliteration of both tibial arteries in their lower third. A biopsy of the left dorsalis pedis artery revealed in microscopic sec-

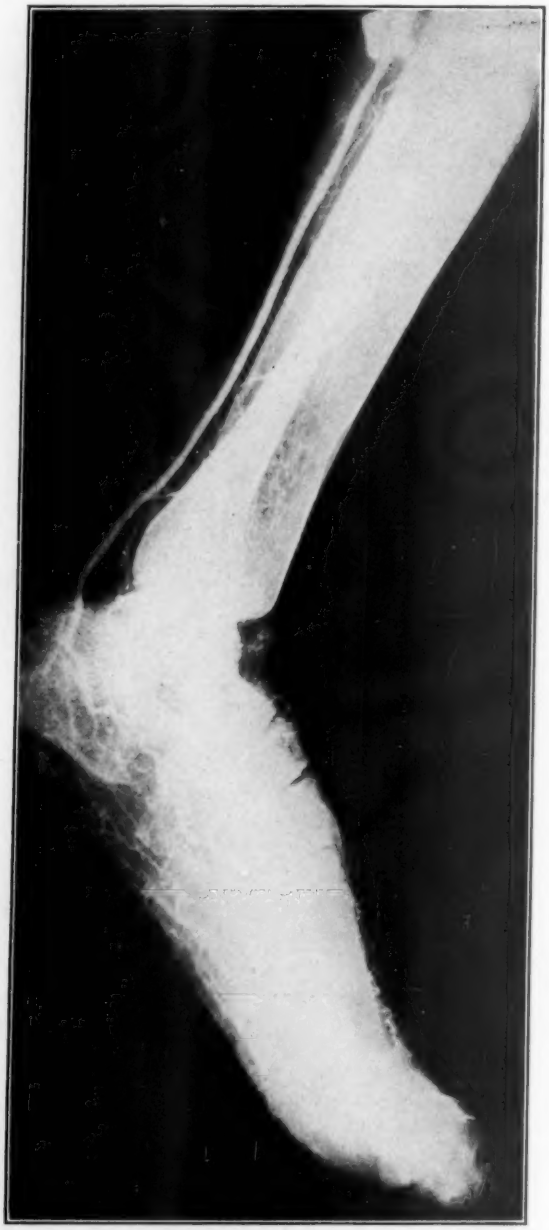

Fig. 13.—Thromboangiitis obliterans (?) in a negro. Occlusion of anterior tibial artery. Gangrene of toes.

tions the lumen completely filled with old fibrous tissue containing a goodly number of small vessels. The media, which was moderately fibrotic, contained a number of new arterioles. The case suggests thromboangiitis obliterans, but that disease

has never been reported in the negro. On the other hand, syphilitic thromboarteritis is a possibility. The patient has been treated for syphilis, and although his Kahn test is negative, he has signs of early aortic regurgitation.

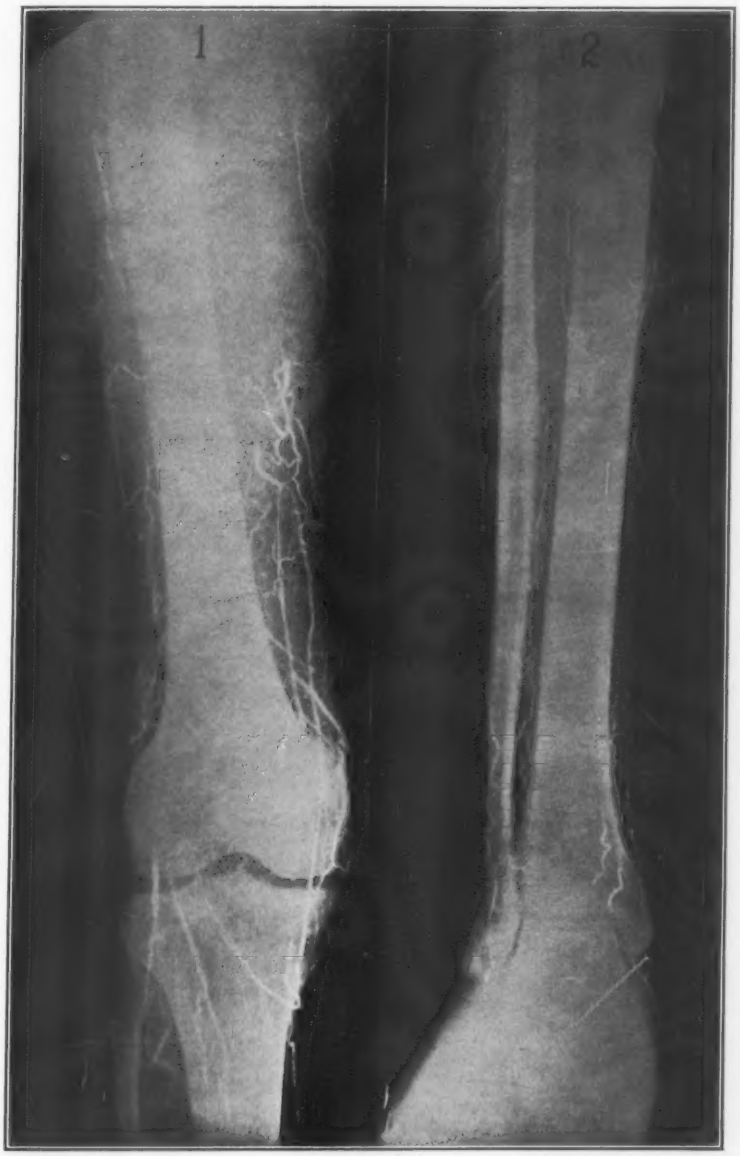

Fig. 14.—Thromboarteritic occlusion of femoral artery and branches. Many long collateral arteries. Gangrene of foot.

Obliteration of All of the Large Arteries of One Lower Extremity.—The most astonishing case is that of a negro, aged thirty-four years, who for three and a half months was suffering from ulceration and gangrene of the fourth and fifth toes of the left foot. He had had a penile lesion one year before, and his Kahn test of the

blood was four-plus. The right lower extremity was clinically normal, but the arteriograms showed evidence of an occlusive process of slight degree in the tibial arteries. The whole left foot was affected by dry gangrene, and there were no pulsations in the arteries of that limb below the femoral triangle. Arteriograms revealed complete absence of shadows of the femoral, popliteal and tibial arteries, but collateral arteries were abundant throughout the thigh and leg (Fig. 14). Amputation was performed below the knee because of the good collateral circulation. There was very little bleeding during the operation, and no large arteries had to be ligated. Some gangrene has occurred in the stump, but amputation has been too recent to permit an estimate of the ultimate outcome. Dissection of the amputated limb showed the tibial arteries to be small fibrous cords. Microscopic sections revealed obliteration of the lumina of the arteries with fibrous tissue and new vessels and vascular canals therein. There were also some deposits of hemosiderin. The media was relatively intact except for secondary changes and some new vessels. The etiology was not clear.

SUMMARY

Thorotrast, a stabilized solution of thorium dioxide, is in most respects an ideal medium for arteriography, and its use has made arteriography a practical and valuable procedure. It has been employed in many cases without apparent harm. The technic is relatively simple, and arterial puncture is not difficult after a little practice. Interpretation of the films requires some experience.

Type of vascular lesion, sites of occlusion, and extent of collateral circulation are readily demonstrable. Perhaps the most practical use for arteriography is to aid in selecting the best site for amputation when gangrene has supervened. However, arteriography does not supplant careful clinical investigation, such as physical examination, thermographic studies, oscillometric readings, and determination of the vasomotor index.

A simple routine method of arteriography has been described. Types of vascular lesions demonstrable by it have been discussed. Typical and unusual cases have been briefly reported and illustrated by photographs of arteriograms.

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THEORETICAL CONSIDERATIONS REGARDING THE VARIATIONS OF THE RS-T SEGMENT AND SUBSEQUENT T-WAVE FOLLOWING LOCAL VENTRICULAR TRAUMA*

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IN A PREVIOUS paper[1] it was shown that a correlation exists between the electrocardiographic curves consequent to artificial stimulation of specific areas on the cat's ventricles and the later RS-T alterations resulting from cauterization of these same areas. From an examination of any one site, it was found that the main initial deflection of the extrasystolic wave was always opposite in phase to that of the RS-T alteration. The purpose of this paper is to demonstrate the significance of the relationship existing between these different portions of apparently dissimilar graphs and to show how conclusions drawn therefrom may be of value in advancing our understanding of the nature of the RS-T deviation and the subsequent T-wave variations following localized ventricular trauma.

THEORETICAL CONSIDERATION OF RS-T ALTERATIONS

In order to explain this inverse relationship regarding the direction of initial extrasystolic waves and subsequent RS-T deviations, it is necessary to review the well-known monophasic electrocardiograms obtained from excitation of injured cardiac muscle strips. This explanation depends upon the fundamental principle, the basis of all the present concepts of tissue activation (Lewis, Craib, Eyster, Macleod), that tissue in an excited state is relatively negative to tissue in a resting state.

As is generally known, upon stimulation of a theoretically uninjured cardiac muscle strip at either end (*1a*, Fig. 1), a diphasic electrocardiogram is recorded in which there is a prominent initial wave, an intervening isoelectric period due to a balance of potential differences, and a terminal wave of lower amplitude whose excursion is opposite to that of the initial wave. The direction of both waves, however, will depend upon the connections with the string galvanometer and upon which end of the muscle strip is excited. Since the end stimulated is the first to manifest negativity, *1b* is recorded when the muscle strip at point *A* is activated and *1c* is recorded when the strip at point *B* is activated. If

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the quiescent muscle strip is injured at *B*, and injured-uninjured lead-offs are taken, a demarcation current or current of injury is recorded (*1d*) which persists so long as dying tissue is present. Upon excitation of any part of this injured strip, a diminution or negative variation of the current of injury now manifests itself. The string, which has been displaced from the isoelectric line by the demarcation current, tends to approach it and a monophasic type of curve *(1e)* is recorded during the excitatory period. The direction of this excursion is constant despite variations in the site of application of the stimulus.[1] Since in the usual operation of the electrocardiograph, constant currents, such as the injury current, are eliminated by the compensation of the string, *1f* is obtained instead of *1e*, and so only the negative variation of the current of injury is ordinarily exhibited *(1f)*.

Certain conclusions can be drawn from a study of these electrograms. In line with the concept that injury to muscle tissue causes similar elec-

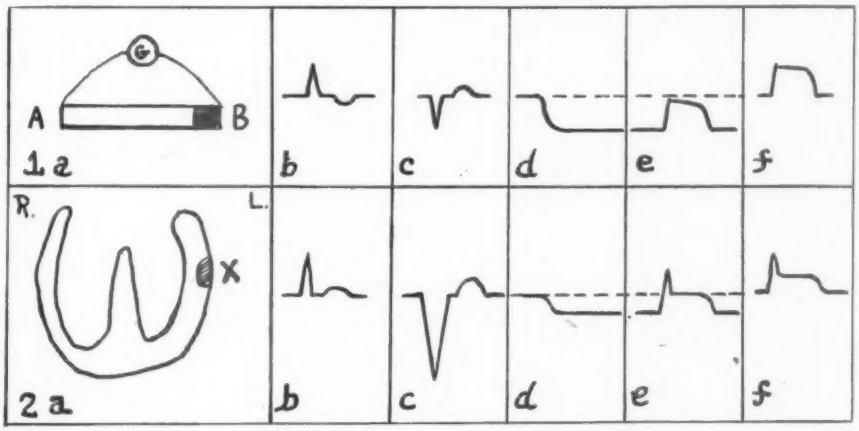

Fig. 1.—In *1a*, the simple cardiac muscle strip *A-B* is so connected to the galvanometer *G* that relative negativity at *A* causes an upward excursion of the string. In *2a*, the frontal section of the heart is connected to the galvanometer by means of the standard indirect Lead I. The deflections are explained in the text. The dashed horizontal line represents the theoretical isoelectric line of the galvanometer. The dark area in each diagram represents the relative size of the injured tissue.

trical reactions as does activation of muscle tissue, it is noted that the initial wave of the electrocardiogram (*1c*), caused by stimulation at point *B* before injury, is in the same direction as the current of injury (*1d*) resulting from trauma to this site (*B*). Since the monophasic wave obtained upon stimulation of the traumatized muscle *(1e)* (or *1f* after compensation) represents the negative variation of the existing current of injury, it is in opposite phase to the simple current of injury *(1d)*; and it, therefore, must be in opposite phase to the initial deflection of the curve (*1c*) obtained by stimulation of the site (*B*) before the injury.

The frontal section of the heart (*2a*) may be regarded as a coiled and distorted thick muscle strip connected to the galvanometer by an indirect lead such as the standard Lead I. Normal cardiac activation is a balance

between almost simultaneous right and left ventricular excitation and, in Lead I, often produces a record such as *2b*. Upon stimulation at *X* on the surface of the left ventricle, a downward initial wave (*2c*) is observed in the electrocardiogram. If it were possible to obtain a record with the heart momentarily free of excitation *2d* would be registered on cauterization at *X*. The direction of this deflection would be negative because the negative pole of the demarcation current is oriented nearer to the left arm electrode. If, after such an injury, normal sinus rhythm is again recorded, *2e* would be obtained, and with string compensation *2f* would be observed.

Comparison between *2b* and *2f* reveals a difference in the contour of the graph consisting of a plateau instead of an isoelectric period between the R- and T-waves. This plateau is recognized as the RS-T change following injury to the heart muscle and is the counterpart of the monophasic type of curve (*1f*) obtained with excitation of the injured muscle strip, and recorded by direct leads. Since, under these conditions, the direction of the RS-T excursion is merely the result of a decrease or neutralization of the fixed demarcation current, it can be seen that the type of deviation is constant regardless of the source of cardiac excitation subsequent to the burn. Samojloff,[2] Parkinson and Bedford,[3] and Crawford and his coworkers[4] have all looked upon the RS-T change as a decrement of the current of injury.

It is evident that the initial wave resulting from stimulation at *X* before the cauterization (*2c*) is in an opposite phase to the RS-T deviation observed after trauma to the same site (*2f*); and furthermore that it is in the same phase as the demarcation current (*2d*). This, therefore, conforms with the theory that both excitation and injury are related electrical processes. There is this difference, however, that while the demarcation current is essentially a local phenomenon, the initial wave of the extrasystole represents the activation wave traveling from the point of stimulation not only through the underlying muscle wall, but also through the remainder of the ventricles. Since the heart may be assumed to approximate grossly a muscle shell (Wilson and his coworkers[5]), the average direction of the excitation wave penetrating from epicardium to endocardium will usually also correspond with its average or resultant direction through the rest of the heart. It can thus be understood why the entire initial deflection of the extrasystole is usually in the same phase as the local demarcation current and in the opposite phase to the subsequent RS-T change.

These theoretical considerations are supported by our experiments[1] in which it was found that the initial extrasystolic waves, obtained by stimulating the heart at any area, were opposite in direction to the RS-T changes recorded after burning the same region. This correlation usually was present for all three leads. Moreover, in the case of the extrasystolic complexes recorded from various sites of stimulation sub-

sequent to the cauterization of any one ventricular site, it was found that there was a displacement in the normally short isoelectric period existing between the initial and terminal deflection. The direction of this alteration depended solely upon the location of the injury, the change in all curves being in the same direction in any one lead, regardless of whether the activation of the heart arose from the sino-auricular node or from any point of stimulation on either ventricle.

COMPARISON OF EXTRASYSTOLES AND RS-T CHANGES IN THE HUMAN HEART

It is realized that the architecture and position of the heart relative to the standard limb leads are not alike in man and in the cat, and that experimental data on electrocardiographic localization of sites of stimulation and cauterization cannot therefore be wholly transposed from one to the other. However, the correlation of extrasystolic curves and RS-T changes, drawn from the observations in the cat's heart, is dependent upon electrical properties inherent in all myocardial tissue and may, therefore, apply equally as well to the human heart.

In order to apply this relationship to clinical cardiac infarction, it is necessary to review the extrasystolic complexes obtained upon excitation of the human heart. Upon stimulation at the left apex anteriorly, Barker and his associates[6] recorded negative main initial ventricular complexes in all three leads, the negativity being least in Lead III. Above this point but still within the lower half of the left ventricle, the complex of Lead III alone became transitional between negative and positive. In accordance with the correlation mentioned above, infarction at the apex of the left ventricle anteriorly would be expected to yield positive RS-T deviations in Lead I and Lead II and possibly in Lead III. With some upward extension of the infarct, RS-T_3 would become isoelectric or even negative. These predicted changes thus seem to conform with the T_1 type of electrocardiogram usually observed with infarction in this region and also with the common variation of the T_1 type.

Upon stimulation of the posterior surface of the human left ventricle, Barker and his coworkers again recorded prominent negative initial extrasystolic complexes in all three leads. An infarction in this region might then be expected to produce RS-T elevations in all three leads. However, the most frequent site of infarction in the posterior wall of the left ventricle is usually near the septum and sometimes the involvement extends partly over to some right ventricular musculature. This site may lie in part to the right of the transitional line for Lead I,* and extrasystoles obtained from here would probably demonstrate isoelectric or

*From a systematic application of stimuli to the epicardial surface of the cat's ventricles, Abramson and Weinstein[7] were able to plot a line of transition for the extrasystolic complexes recorded in Lead I. The initial extrasystolic complexes were positive to the right of the line and negative to the left of the line. This line, running almost vertically down over the anterior surface of the heart and then curving around the apex to extend upward over the posterior surface, was situated on the left ventricle near the septum in most of its course.

even positive initial complexes in Lead I. Hence it can be seen that an electrocardiogram of infarction in the latter region would reveal elevation of RS-T_2 and RS-T_3, whereas RS-T_1 might be isoelectric or even negative. It is evident that such a graph is similar to the clinical T_3 type of record obtained with the most frequent site of infarction in the posterior wall of the left ventricle.

Certain inferences may be drawn about localization of clinical myocardial infarction if the data obtained in the cat's heart are more broadly applied. In anterior infarction the RS-T_3 displacement depends upon the caudocephalic relationship of the infarct in the left ventricle, cephalic extension producing a negative RS-T_3 and caudal localization producing a positive RS-T_3. In anterior infarction of the left ventricle RS-T_1 and RS-T_2 are usually positive. In posterior infarction the RS-T_1 displacement depends upon the extent of the infarction to the right or left of the line of transition for Lead I, mentioned above, extension to the right yielding a negative RS-T_1. RS-T_2 and RS-T_3 are ordinarily positive in posterior infarction of the left ventricle. Accordingly, the frequently observed reciprocal relation of RS-T_1 and RS-T_3 displacements in individual clinic records appears to us to be merely fortuitous.

THE VARIATIONS OF THE T-WAVE FOLLOWING MYOCARDIAL INFARCTION

It is readily appreciated that the RS-T deviation from the isoelectric line persists only so long as the current of injury endures. In patients with myocardial infarction, the subsequent electrocardiograms during a temporary interval of weeks or even months usually reveal a prominent coved and peaked T-wave, whose direction is opposite to that of the previous RS-T alteration. This sequence may be explained by a further application of the theoretical considerations presented above.

With vascular occlusion the injured myocardium manifests a current of injury only during the initial stage of degeneration, since dead muscle fibers are electrically inert. As healing in the infarct occurs, the absolutely destroyed muscle becomes replaced with fibrous tissue, and the other part returns to a normal state sooner or later. As Parkinson and Bedford[3] have remarked, there exists in all probability a zone of transition, exhibiting impaired circulation, between the normal myocardium and the site of actual necrosis. It is reasonable to assume that in this intermediate zone, the zone of reactive inflammatory changes, there may be some impairment of myocardial function with a concomitant delay in the electrical processes of both activation and retreat.

Delay in retreat in this transitional zone may account for the coved or "coronary" T-wave. The comparatively low voltage of the normal T-wave is the result of a partial balance, and the preceding isoelectric interval a result of complete balance, of opposing electropotentials exist-

ing simultaneously throughout the major portion of the heart during the recovery period. As Katz[8] has pointed out, the actual direction of the T deflection is probably determined by that part of the heart in which the electropotential endures the longest. When any pronounced local retardation in recession appears, its electrical effects are practically unopposed by those of earlier retreat in the rest of the heart; and one of the possibilities of such an imbalance is the production of a T-wave of greater magnitude and of different contour and direction. It is reasonable to assume that the negative potential in the activated muscle mass would persist longest in the intermediate zone with impaired circulation, discussed above, and that the "coronary" T-wave would therefore be due to the delayed and consequently unopposed electropotential present in this zone. Furthermore, since the direction of the original current of injury was also the result of negative charges in the same location and orientation, it follows that its theoretical registration and that of the "coronary" T-wave would both be in the same phase. Since the RS-T alteration obtained during the acute stage was a decrement of the current of injury and thus in opposite phase, it can be understood why the direction of this RS-T alteration similarly is inverse to that of the subsequent "coronary" T-wave.

To illustrate this relationship and to demonstrate that the theory of doublets and their limited potential differences may also apply, a specific area of the heart, such as the apex of the left ventricle, will be considered. Because of the site chosen, the normal potentials of excitation and retreat travel downward and to the left through this region. If it were possible to record only their local electrical effects, the initial deflections (representing excitation) would be positive, and the terminal deflections (representing retreat), negative in at least Lead I and Lead II. At this site the initial deflection of Lead III would be either positive or negative, and, hence, for simplicity, this lead is not included.* It is generally known that acute infarction of the apex of the left ventricle produces RS-T elevations in the first two leads and subsequent T-waves which are negative. The direction of these T-waves is, therefore, similar to that of the above mentioned terminal deflections normally arising from this local site during retreat. In consequence thereof, the "coronary" T-wave is necessarily due to a predominance of the recovery factor in this region caused, most likely, by the delay in retreat incident to the infarction here.

Craib[9] has made the assumption that the "coronary" T-wave is due to the entire absence, during recovery, of the normal electrical effects in the infarcted region. If this were so, then the balance during re-

*With the customary Einthoven equilateral triangle constructed from the three standard leads, an excitation vector directed downward and to the left produces positive projections on the lines of Lead I and Lead II. The projection on the line of Lead III is either positive or negative, depending, respectively, upon whether the vector is oriented clockwise or counterclockwise to the perpendicular of the line of Lead III. With the reversal of the charges of the advancing doublet during the period of recession, a recovery vector directed downward and to the left produces negative projections on the lines of Lead I and Lead II.

covery would swing in the opposite direction; and with the normal negative terminal components of Lead I and Lead II missing from the infarct at the apex of the left ventricle, the "coronary" T-waves would become more elevated than the normal T-waves, and thus be recorded in the same direction as the previous RS-T alterations. Craib's assumption in reference to the usual "coronary" T-waves of several weeks' duration accordingly does not seem applicable. The most satisfactory explanation for the origin of the "coronary" T-wave, it seems to us, is that it is a result of the retardation of recovery in the living muscle tissue with impaired nutrition, lying in the zone between the actual necrosis and the normal heart muscle. With the return of metabolic conditions in this intermediate zone to normal, the "coronary" T-wave gradually may become replaced by a normal T deflection.

However, curves of acute infarction, showing large T-waves in the same phase as RS-T alterations and occurring for a short time after the acute insult, have been reported and can be explained by the supposition that part of the affected myocardium is in a state of shock and consequently inert electrically, while the other more severely damaged part produces only the current of injury.

SUMMARY

1. The theoretical basis is presented for the correlation, observed in the cat's heart, that the initial deflection of the extrasystolic wave, recorded with artificial stimulation upon a specific site, is in opposite phase to the RS-T change, recorded with cauterization of the same site.

2. This correlation seems applicable to the human heart. It may explain the variations in the relationship of the RS-T displacement in the first and third leads.

3. The usual characteristic T-wave of myocardial infarction is probably the result of a retardation of the process of retreat in the living muscle tissue with impaired circulation, lying in the zone between the actual nerosis and the normal heart muscle.

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APPLICATION OF ROENTGENKYMOGRAPHY TO THE STUDY OF NORMAL AND ABNORMAL CARDIAC PHYSIOLOGY*

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ROENTGENKYMOGRAPHY is a method of recording graphically visceral movement by the x-ray. The technic and the general principles of application of this method to the study of the heart have been dealt with in other communications.

Roentgenkymography of the heart gives a record similar to that obtained with the myocardiograph in animal experiments. Both inscribe cardiac movement, but the roentgen method, utilizing a beam of x-ray instead of a mechanical lever, gives a record which is freer from distortion.

The kymoroentgenogram of the heart is made by interposing between the patient and the film an impermeable sheet of metal in which there are slits 0.4 mm. in width, spaced 12 mm. apart. The film is not stationary as in the ordinary roentgenogram, but moves at right angles to the direction of the slits during the exposure. Actually the movement of only those portions of the heart surface are recorded which are opposite the slits, thin bands 0.4 mm. wide and 12 mm. apart. This spacing is, however, sufficiently close to give information regarding all those portions of the heart which contribute to the make-up of the cardiovascular shadow. To avoid overlapping of the records, the film is moved just short of the distance between the slits (Fig. 1). The film is standardized to move 12 mm. per second, and the exposure is one second, thus recording one or more complete cycles. The time may be read on the distance axis.

If the movement of that portion of the heart shown in the slit is more or less parallel to the direction of the slit, it is recorded in the form of a wave. If the point has no movement or if the movement is at right angles to the direction of the slit, the contour shows a straight edge without waves.

The form of the wave with a definite rate of film motion depends on the character of the movement of the particular point of the heart. The legs of the waves may be straight or curved depending on the speed of motion. A very sharp peaked wave is produced by an extremely rapid movement and change in direction. The movement may be so fast that its record is practically a horizontal line. A domelike wave represents

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a slow change in direction, a progressive increase and diminution in the speed of movement—a motion similar to that of a swinging pendulum. When the to-and-fro motion is not regular, the motion being faster in one direction, the faster motion produces a straightening and shortening of the particular leg of the wave. Imposed on these waves are angulations, hooks, peaks, indentations, and terraces, representing the rapid changes in the direction of the movement of the cardiac muscle, movements of the heart as a whole, and local vibrations produced by currents of blood within the heart.

It is obvious that the outward thrust of the heart action (diastole) produces one side of the wave and the inward thrust (systole), the other. The crest of the wave represents the end of diastolic period or

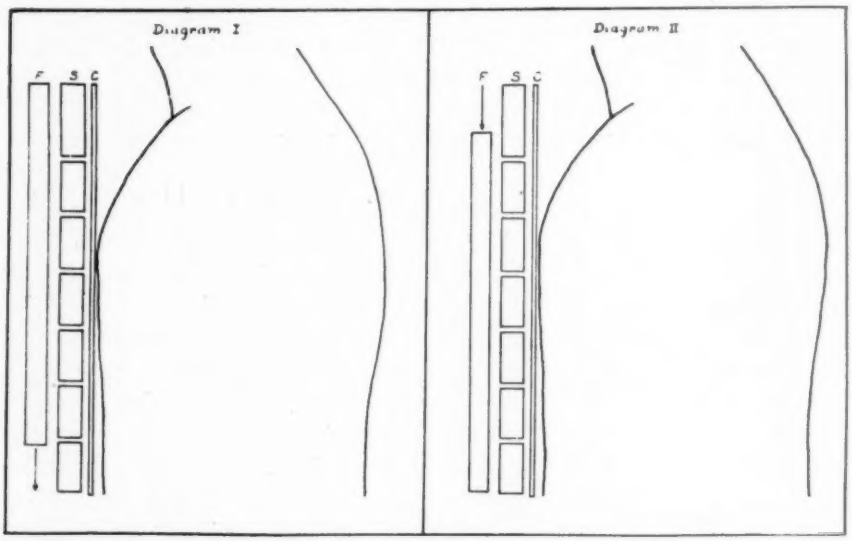


Fig. 1.—*S*, lead sheet with slits; *F*, cassette and film which move downward a distance slightly less than the distance between slits. Diagram I, before exposure, and Diagram II, after movement of the film and its exposure.

beginning of systolic, while the deepest portion of the trough represents the period of maximum systole or the beginning of diastole.

Since the film moves downward, the flow of the time is upward. The waves differ in morphology depending on the chamber of their origin. The altitude of the wave represents more or less accurately the amplitude of movement; the abscissa the duration of movement. Recorded during the same fraction of time, the time relationships of the various waves are directly comparable. The analysis of the time relationships is limited by a time resolution of 0.02 sec.

Figure 2 is a typical kymogram of a normal heart. It is obvious that the waves differ in appearance over different parts of the cardiac shadow and are characteristic for each chamber, thus providing a method for topographic analysis of the cardiac contour. It is not necessary to en-

ter here in detail into the contribution which this method of examination makes to the analysis of the composition of the cardiac silhouette. It is sufficient to point out that, contrary to the usual x-ray and anatomical interpretation, the right ventricle appears to participate in the formation of the lowermost portion of the right cardiac contour in a large proportion of normal hearts. Definite ventricular waves practically similar to the ventricular waves on the left side have been found in 75

Fig. 2.—Roentgenkymogram of a normal heart. The waves over the entire cardiac shadow are movement records of the particular portions of the heart and its great vessels. The peak of the wave represents the particular part in maximum diastole or dilatation while the deepest point in the valley represents the position of the particular part in maximum systole or retraction. Waves of different shape and size may be distinguished over different portions of the cardiovascular shadow, corresponding to the chamber of their origin. Since the duration of the x-ray exposure is one second, the distance between the black lines may be divided into as many parts as is desired representing fractions of a second. By laying off on the waves of each band a definite distance, corresponding to a certain fraction of time and connecting these homologous points, the shape and outline of the heart at that particular instant may be shown.

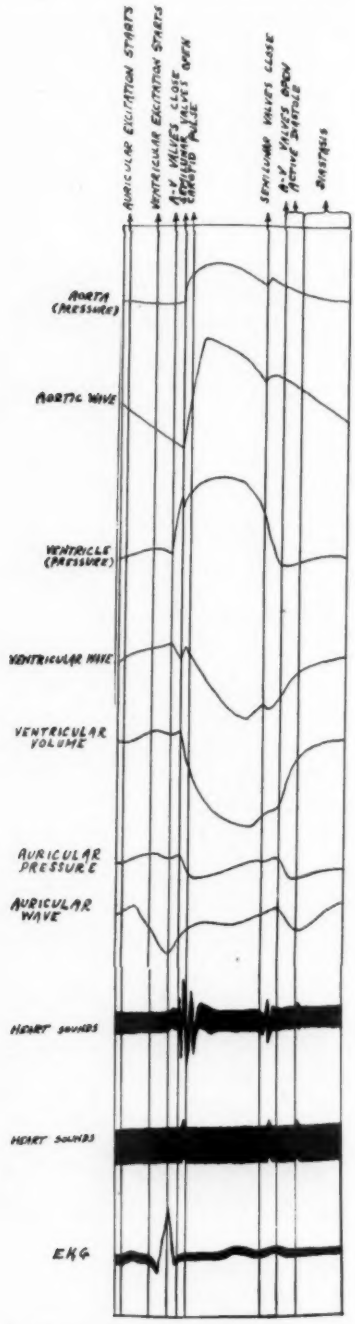


Fig. 3.—Diagrammatic representation of relation of kymographic wave record to the record of other events of the cardiac cycle. The movements of the different chambers may be graphically correlated and the relation of the kymographic waves to each other and to other events in the cardiac cycle. The time relations of the kymographic waves have been checked with simultaneously recorded electrocardiograph and heart sounds and on this basis the waves may be assigned to specific events in the cardiac cycle. In fig. 5 is a graphic correlation of the waves of various chambers with a simultaneously recorded electrocardiograph.

per cent of young adults. Further, the portion of the cardiac contour above the right auricle is generally taken to represent the ascending aortic arch. However, in 180 normal hearts, aortic waves were present in only 20 per cent. In the majority of cases this portion of the cardiovascular contour is apparently formed by the superior vena cava.

The movements of the different chambers may be graphically correlated by charting the relationship of the kymographic waves to each

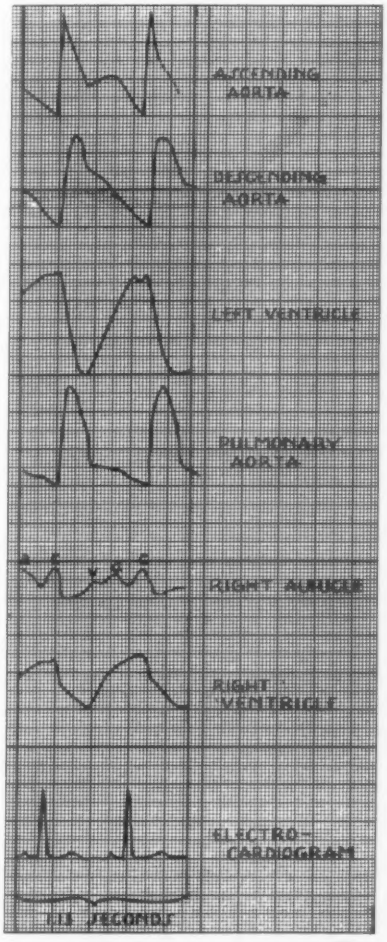


Fig. 4.—Graphic correlation of kymographic waves from a normal kymogram.

other and to other events in the cardiac cycle on the same time axis as is diagrammatically represented in Fig. 3. The time relations of the kymographic waves have been checked with simultaneously recorded electrocardiogram and heart sounds, and on this basis the waves may be assigned to specific events in the cardiac cycle. Figure 4 is a graphic correlation of the waves of the various chambers, with a simultaneously recorded electrocardiogram.

VENTRICULAR WAVES

This wave consists fundamentally of a sharp, smooth inward limb representing systole, followed by a bent limb representing diastole. The amplitude of the wave does not, however, always represent the true amplitude of motion of the particular point of the ventricular contour. The kymogram records accurately only that component of motion parallel to the slit; movement at an angle to the slits is somewhat distorted and exaggerated.

If the motion is not parallel to the direction of the slits, as is the case with the greater portion of the left cardiac border, particularly in cases in which the upper part of the contour runs very obliquely to the direction of the slits, the amplitude may be determined by projecting corresponding peaks and troughs of two bands to the horizontal line bounding each band and connecting these projections. The perpendicular distance between these lines is the amplitude, but not the exact amplitude, for with a target-film distance of 100 cm. there is still some magnification of the image.*

The ventricular wave bears a close resemblance to ventricular volume curves experimentally recorded with the cardiometer. Some, impressed by the close correspondence, regard the kymographic wave of the left ventricle as practically a pure volume curve, and with restrictions accept differences in amplitude of the wave as indices of the changes in stroke volume. Quantitatively, however, the change in cardiac contour, which the kymogram records, is not purely a volume change, but is the resultant of the predominant contractile thrust, of rotary movements, and of motion of the heart as a whole. Besides this there is the motion of the atrioventricular septum which is not at all represented in the movements of the outer contour.

This criticism applies, of course, not only to the kymographic, but to all x-ray technics of studying cardiac motion, viz., fluoroscopy, cinematography, and systole-diastole exposures, and reveals the fundamental inaccuracy of attempting to estimate changes in heart volume from changes in the area of the cardiac shadow as has been advocated by Bardeen[1] and by Eyster and Meek.[2]

The diastolic limb of the ventricular wave (Fig. 5) at ordinary resting rates of from sixty to eighty shows a break at about its middle, the later half of the wave being somewhat flattened. The first major segment of the diastolic limb corresponds to the period of early rapid inflow. The break in the limb indicates a reduced rate of filling, i.e., the period of diastasis preceding contraction. Auricular systole, which occurs during this period of diastasis, does not usually modify perceptibly the diastolic wave and does not appear to contribute significantly to

*While the shorter focal distance prevents teleroentgenographic measurements, it nevertheless has the advantage of emphasizing by slight magnification the more delicate and less perceptible portions of the wave.

ventricular filling, although occasionally a distinct outthrust on the diastolic limb may be observed simultaneously with the inthrust of the auricular wave. When the heart rate is rapid, the break in the diastolic limb disappears; there is no period of diastasis; and the filling continues uninterruptedly to the beginning of the next systole. Under these circumstances auricular systole contributes significantly to the filling of the ventricle, for the ventricle is not yet full when auricular systole takes place.

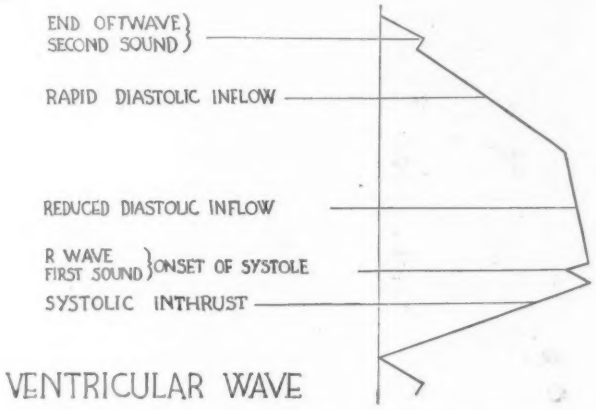


Fig. 5.—Graph showing the relationship of movement to conduction phenomena.

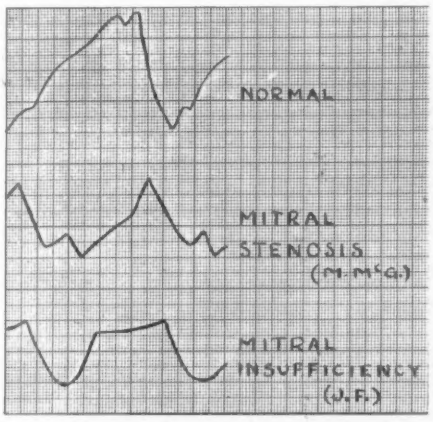


Fig. 6.—Graph transposed from kymograms showing the waves of left ventricle in the normal state, in mitral stenosis, and in mitral insufficiency.

The rapid inflow into the ventricle in early diastole occurs as a consequence of the accumulation of blood in the auricle during the ventricular systole while the atrioventricular valves are closed. When the valves are opened, the inflow into the ventricle takes place with a sharp sudden fall in auricular pressure.

In mitral insufficiency the first dynamic event is congestion in the left auricle, which precedes further back pressure effects into the pul-

monary artery, right heart, and great veins, the mean pressure in the pulmonary artery usually not being measurably affected (McCollum and McLure[12]). When the insufficiency is uncomplicated, the pressure in the left auricle is increased markedly during ventricular systole because of the regurgitation. The rate of inflow into the ventricle in early

Fig. 7

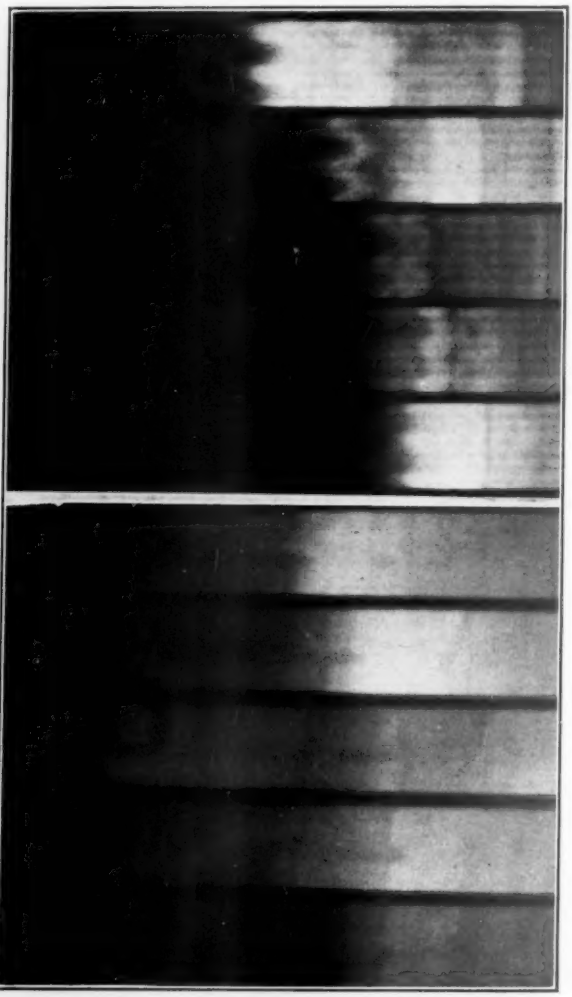


Fig. 8.

Fig. 7.—Mitral insufficiency, ventricular filling abrupt and almost completely in early diastole. Clinically diagnosis of mitral stenosis was made on basis of loud systolic and diastolic murmurs at apex, with presystolic murmur and thrill at mitral area. Post-mortem examination revealed a greatly widened mitral ostia with no evidence of any stenosis.

Fig. 8.—Mitral stenosis. Delayed filling of left ventricle, most of filling occurring at end of diastole due to auricular systole. The ventricular movement is of small amplitude. Typical buttonhole mitral stenosis found at autopsy.

diastole is accordingly accelerated. There is practically complete filling in the early inflow phase. This, as pointed out by Hirsch, is revealed

in the ventricular wave by a rapid, outwardly directed limb in the early inflow phase of diastole. It is succeeded by a long period of diastasis. The two phases of the diastolic limb are thus differentiated by a sharp angulation (Fig. 6).

In mitral stenosis, on the other hand, although the left auricular pressure is also increased, early diastolic inflow is impeded because of the narrowed atrioventricular orifice, and the filling is slow and gradual throughout diastole, with no period of diastasis (Fig. 6). Under these circumstances, auricular systole may contribute significantly to ventricular filling. The diastolic limb of the ventricular wave is an unbroken line of low amplitude and attains its maximum height late in diastole.

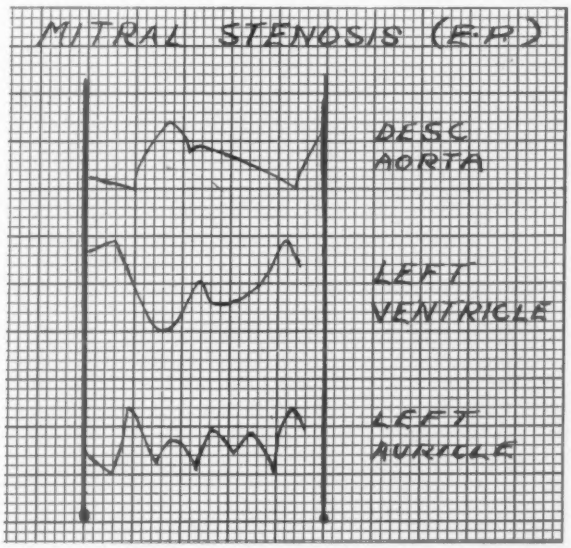


Fig. 9.—Mitral stenosis. Graph showing the typical late ventricular filling and the diminished aortic movement.

When both lesions coexist, the filling curve varies from the insufficiency to the stenotic type depending on which process predominates. It is generally known that detection of an organic stenotic lesion as evidenced by a diastolic apical thrill and murmur does not necessarily signify dynamic mitral stenosis. The characteristic dynamic changes are, according to Wiggers, produced only by excessive degrees of stenosis, a very considerable degree of narrowing (approximately to one-quarter natural size), being required before the increase in resistance fails to be compensated for by the rise of left auricular pressure which naturally follows.

The kymographic examination may thus assist in the clinical differentiation of the dominant lesion, in the presence of signs indicating

double mitral disease. In Figs. 7 and 8 are reproduced the ventricular kymographic waves of two cases, each clinically diagnosed as double mitral disease. The kymographic diagnoses based on the study of the waves of the left ventricle, in one, of mitral insufficiency (Fig. 7), and in the other, of mitral stenosis (Fig. 8), were confirmed by autopsy.

The graphic transcription in Fig. 9 illustrates clearly the delayed filling of the left ventricle in mitral stenosis; the case being that of

Fig. 10.—Kymogram. Mitral insufficiency.

a thirty-three-year-old woman, with a twenty-eight-year history of rheumatic activity, presenting all the clinical features of mitral stenosis.

Figure 11 shows a graphic correlation of the waves from a kymogram of advanced mitral insufficiency (Fig. 10). The left auricle is markedly dilated, occupying a considerable portion of the left contour. The ventricular wave shows the accentuated early diastolic inflow characteristic of mitral insufficiency, followed by a long period of reduced filling. During ventricular systole the auricle is seen to fill to a greater degree

than normal, because of the regurgitation. The auricular waves otherwise resemble the right auricular waves found normally. The systolic outthrust of the aortic wave in this case is considerably slower than normal, indicating a reduced rate of ejection. This, according to Wiggers,[17] is the dynamic crux of mitral regurgitation, a heart remaining compensated in the face of a mitral leak so long as it is able to attain a

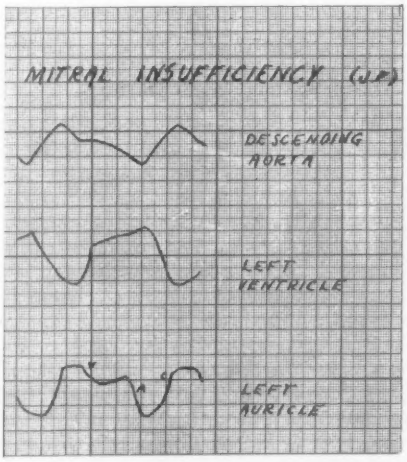
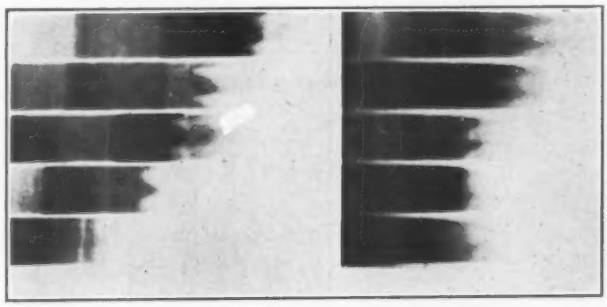


Fig. 11.—Graph from kymogram shown in Fig. 10, showing correlation of aortic, ventricular and auricular waves. The graph shows almost complete filling of left ventricle in early diastole, marked increase in left auricular volume coincident with systolic inthrust of the left ventricle and slow systolic outthrust of aortic wave as in aortic stenosis due to diminished rate of ventricular discharge into the aorta in consequence of mitral regurgitation.



A. *B.*

Fig. 12.—Development of mitral insufficiency in a child of eleven years. *A*, normal kymogram, taken upon admission for first attack of rheumatic fever.

B, mitral insufficiency, six months later, showing ventricular wave characteristic of mitral insufficiency.

rapid rise of pressure isometrically and maintain a normal rate of discharge, decompensation setting in when a weakened myocardium cannot contract forcibly enough to raise its pressure rapidly, the pressure being dissipated through the mitral valve due to the regurgitation, with consequent diminished rate of discharge into the aorta.

The development of mitral insufficiency recorded kymographically, paralleling the clinical course, is shown in Fig. 12, *A* and *B*. The first kymogram, taken shortly after admission for a first attack of rheumatic fever, is normal, but the second, six months later, shows a decided modification of the wave of the left ventricle which indicates that the ventricle fills abruptly early in diastole and that this is followed by a long period of diastasis giving the wave the appearance characteristic of mitral insufficiency.

Superimposed on the main limbs of the ventricular wave are two small serrations. One is located immediately after the end of systole, appearing usually as a step at the beginning of the diastolic limb. This corresponds in time exactly with an incisura on the retracting limb of the aortic and pulmonary artery waves. The other serration is located at the peak of the ventricular wave, at the beginning of the systolic

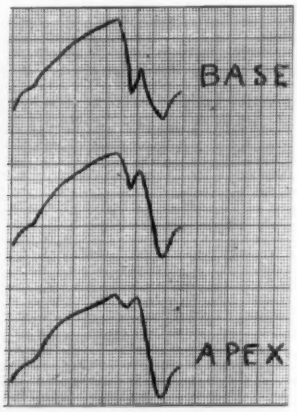


Fig. 13.—Variation of the ventricular wave from base to apex. The actual time of closure of the A-V valves is the same, but there is apparently a more vigorous movement at the base.

limb (Fig. 5). These serrations have been shown by Hirsch and Schwarzschild[7] to correspond exactly with the second and first heart sounds, respectively. Since the sounds are related to valve action, it appears likely that these waves are related to closure of the semilunar and atrioventricular valves.

The steplike serration simultaneous with the second heart sound at the beginning of the diastolic limb and corresponding precisely in time with the incisural notch of the vascular waves terminates simultaneously with the deepest point of the incisura, which marks the closure of the semilunar valves (Fig. 3).

The constant appearance of the serration as an outward step at the beginning of the diastolic limb and its simultaneity with the second heart sound and with the vascular incisura suggest that a perceptible regurgitation may take place physiologically at this time, i.e., before

the closure of the semilunar valves. Further evidence for this view is afforded by the fact that in aortic insufficiency this initial outward limb is greatly accentuated, appearing no longer merely as a small step engrafted on the main diastolic limb, but as a definite peak.

The serration simultaneous with the first heart sound appears as a double peak with an intervening notch, the total duration of this complex being about 0.08 sec. It is located essentially at the peak of the ventricular wave but undergoes progressive modification from the base to the apical portion of the ventricular contour, as seen in Fig. 13. Toward the base of the heart, the second peak is located on the systolic limb; over the middle and apical portion of the ventricular border, it lies closer to the apex of the ventricular wave. The time of this second

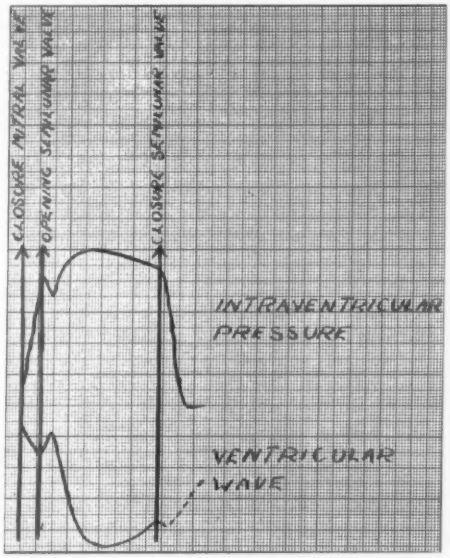


Fig. 14.—Correlation of ventricular kymographic wave with intraventricular pressure curve.

peak is the same over all portions of the ventricle despite changes in position. The trough between the two peaks is simultaneous with the onset of ejection as measured by the beginning outthrust of the aortic wave.

This complex cannot represent volume changes, for the first inward movement occurs during the isometric phase of the systole and simultaneous with the major component of the first heart sound, before ejection has begun. These rapid movements do, however, parallel and appear to reflect the changes in intraventricular pressure which occur at the onset of systole (Fig. 14).

During the isometric phase of systole there is a sharp rise of intraventricular pressure which transiently overshoots the aortic pressure due to inertia in the opening of the semilunar valve. With the opening of

the semilunar valve there is an abrupt decline to aortic pressure, the intraventricular pressure thereafter following aortic pressure for the remainder of systole.

The isometric overshoot of intraventricular pressure above aortic pressure appears to be directly proportional to the vigor of ventricular contraction, the overshoot disappearing in a weak ventricle, due to the lessened rate of increase in intraventricular pressure isometrically, giving the semilunar valve time to open before the aortic pressure is exceeded. It is significant that in myocardial degeneration the corresponding spike of the ventricular serration is greatly diminished or absent. It is also lost in mitral insufficiency where the regurgitation prevents an abrupt rise of intraventricular pressure.

The same sort of vibrations have been described by Tennant and Wiggers[16] experimentally with the myograph. This, however, is believed by them to be an artefact. It is interesting to note that in their myograms showing the development of myocardial damage following coronary occlusion these serrations disappear. Tennant and Wiggers suggest, consistent with the explanation offered above, that a local area of weakness may cause significant loss in the development of intraventricular pressure.

AURICULAR WAVES

The waves produced by auricular motion are multiple and of small amplitude. If the waves are graphically correlated with ventricular and vascular waves (Fig. 4), a definite sequence in their relation to ventricular and vascular waves is observed, which is constant not only in the same subject in different segments, in successive beats, and on different days, but in different subjects as well.

The left auricle is represented in the kymogram only by the auricular appendix which most often occupies but one segment, and the motion of the left auricle is therefore not well reflected, except in pathological dilatation in mitral disease.

The right auricular motion is far more constant, and there are typical waves over this portion of the cardiac contour. The information given by these waves is the same as may be obtained from auricular pressure records in animals and jugular pulse tracings in man.

The first of the auricular waves appears as an inthrust terminating at the peak of the ventricular wave immediately preceding the onset of systole. It is simultaneous with the P-wave of the electrocardiogram (Fig. 4) and represents auricular systole. Its onset comes at about the peak of the P-wave and the duration varies from 0.08 to 0.12 sec. (a).

The second wave begins as a sharp outthrust with the onset of the isometric vibration complex of the ventricular wave which is simultaneous with the first heart sound. This wave is due to a reflection of ven-

tricular events. This outward motion in early systole corresponds to the abrupt rise in auricular pressure at the onset of the ventricular contraction which is due to back pressure from the ventricle in the closure of the atrioventricular valve. The immediately succeeding fall in auricular volume parallels a reduction in auricular pressure which Wiggers ascribes to a descent of the base of the ventricle, the brusque auricular traction reducing the pressure (e).

Following this inward thrust the auricle gradually increases in volume for the remainder of ventricular systole, as a result of inflow from the great veins. With closure of the semilunar valves, as indicated by the aortic incisura and ventricular serration corresponding to the second heart sound and the opening of the A-V valve, the auricular volume decreases sharply, corresponding to the rapid inflow phase into the ventricle (v).

The upper portion of the right cardiac contour is formed in the majority of cases in the young, not by the ascending arch of the aorta, but by the vena cava. In clear records in which the waves of the vena cava have sufficient amplitude to be analyzed, they closely parallel the auricular waves, with a time delay of a few hundredths of a second, which may be progressively traced, because of transmission of the impulse from the auricle up the vena cava (Fig. 18). The same three waves can be distinguished, and they form the a-, c-, and v-waves recorded in jugular pulse tracings. The kymogram thus confirms the now generally accepted interpretation of the origin of the c-wave of the jugular pulse, i.e., that it is due to transmission from the auricle and is not, as MacKenzie originally believed, a parasitic wave reflected from the carotid artery by reason of the close apposition of the jugular vein and carotid artery.

VASCULAR WAVES

The aortic wave consists of a sharp outthrust commencing simultaneously with the beginning of the systolic limb of the ventricular wave, succeeded by a blunt peak whose retraction terminates in the incisural notch. The onset of ejection is marked not only by the outthrust of the aortic wave, but a coincidental sharp increase in density of the aortic shadow as well. The time from beginning aortic outthrust to the depth of the incisural notch forms a convenient measure of the duration of ejection since it represents the time from the opening to the closure of the semilunar valves. There is a slight rebound from the depth of the incisural notch after which a gradual recession of the aortic wave takes place throughout diastole. Correlation with the electrocardiogram (Fig. 4) shows that the QRS complex is completed a few hundredths of a second before the onset of ejection, as evidenced by the beginning aortic outthrust.

The end of the T-wave closely approximates the incisura, but the correlation is not precise, as it may either precede or follow it by 0.03 sec. in the same subject.

The aortic wave bears a striking resemblance to arterial pressure curves, and the changes in aortic volume represent, in fact, changes in lateral arterial pressure, although giving no information as to the absolute magnitude of the aortic pressure. It is really the same as a subclavian sphygmographic tracing which also records changes in arterial volume as a measure of pressure changes throughout the cycle,

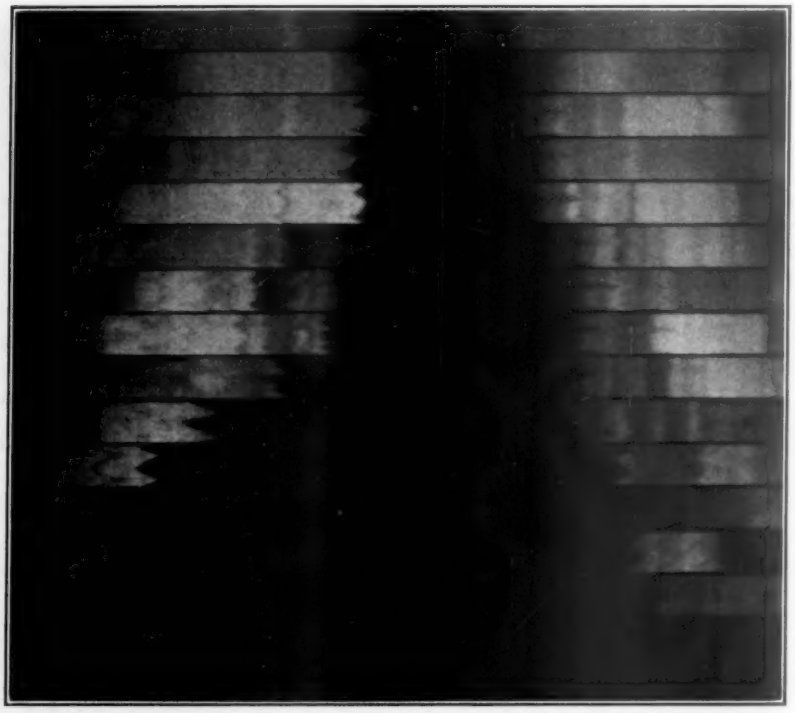


Fig. 15.—Kymogram of a case of aortic insufficiency. Note the high peak of the second sound wave at the base of the diastolic limb of the ventricular wave and the primary collapse of the aortic wave.

but the kymogram possesses the advantage over the sphygmogram of being a direct and not an indirect method of registration.

The amplitude of the aortic wave, usually of the order of 0.5 cm., may thus be taken as a measure of lateral arterial pulse pressure provided that arterial elasticity is unchanged. The aortic wave provides a measure, in the same manner, of arterial elasticity, based on the excursion of the aortic wave per unit change in pressure, although quantitative application of this principle would first necessitate thorough standardization. A gross illustration of diminished arterial elasticity revealed in the aortic wave may, however, be seen in Fig. 16, No. 3,

where, despite a large pulse pressure associated with aortic insufficiency, the aortic wave is of very low amplitude. In this case there were sclerosis and calcification of the aortic arcus.

The waves of the ascending and descending aorta differ both in time relationships and in form. There is a measurable time delay between the beginning outthrust of the ascending and the descending arches of the aorta, averaging 0.03 sec., which is due to transmission of the pulse

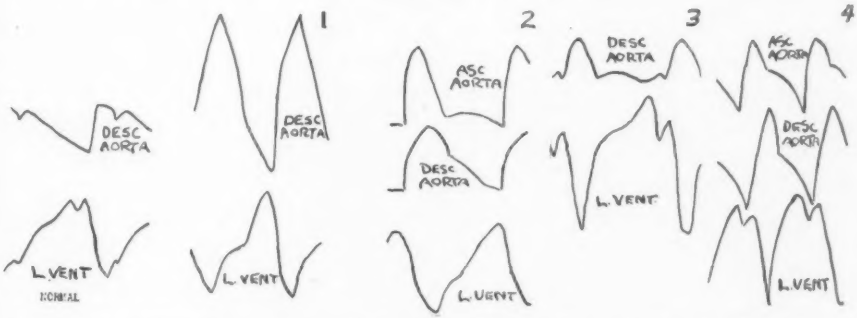


Fig. 16.—Ventricular and aortic waves in aortic insufficiency. These tracings reproduce the aortic and ventricular waves of several cases of aortic valvular disease. Definite changes in the aortic curve may take place in aortic insufficiency. The amplitude of the wave is greatly increased corresponding to the increase in pulse pressure. In contrast to the gradual retraction succeeding the peak, interrupted by a moderate incisural notch, which is seen in normal cases, the retraction succeeding the peak is greatly accentuated so that there is almost complete incisural collapse of the wave, and the aortic pressure is not sustained, being not much higher at the end than at the beginning of ejection. These changes are much more pronounced in the ascending than in the descending aorta. If the regurgitation is not severe the aortic wave approaches closely to normal. The amplitude of the ventricular waves are exaggerated in aortic insufficiency. This represents the increased systolic output of the left ventricle necessary in aortic insufficiency to maintain a normal circulating minute volume.

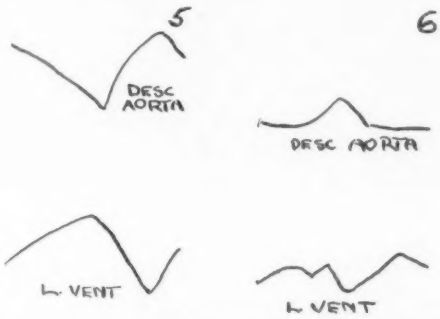


Fig. 17.—Tracing 5 shows the aortic and ventricular waves of a case of well-marked aortic stenosis (80/60). The waves are in striking contrast to those seen in aortic insufficiency. The outthrust of the aortic wave is very slow and gradual, with attainment of a late peak because of the reduced rate of ejection. The systolic limb of the ventricular wave likewise is slower than normal, and the amplitude of the ventricular wave is considerably less than in aortic insufficiency. These observations duplicate the findings in experimentally produced aortic stenosis using intraventricular and aortic pressure curves.

wave. The distance between the two points of measurement is about 6 inches. This would give a velocity in the aorta of about 17 feet per second, which is of the same order of velocity as is found in determinations by subclavian and femoral sphygmograms. The range of error

over this short segment is so great, however, that at best only a crude indication of actual pulse wave velocity is obtained by this method.

Not only is there a time delay from the ascending to the descending aorta but the form of the wave changes. In the descending arch of the aorta the aortic pressure rises steeply with the onset of ejection, the rate or rise gradually diminishing with attainment of a peak at about midsystole. The curve then falls slowly with an appreciable retraction at the end of the ejection, which is halted by closure of the semilunar valves. In the ascending aorta the initial rise with the onset of ejection is much more abrupt and is practically linear. A sharp peak is attained within a few hundredths of a second in contrast to the blunted peak later in point of time in the descending aorta. The retraction succeeding the peak is much greater, but there is little rebound, so that the incisural notch is not usually as well marked.

Definite changes in the aortic curve may take place in aortic stenosis and insufficiency. In Figs. 16 and 17 are reproduced the aortic and ventricular waves of several cases of aortic valvular disease. In aortic insufficiency the amplitude of the wave is greatly increased, commensurate with the increase in pulse pressure. In contrast to the gradual retraction succeeding the peak, interrupted by a moderate incisural notch, as seen normally, the retraction succeeding the peak is greatly accentuated so that there is almost complete collapse of wave. The aortic pressure is not sustained, being not much higher at the end than at the beginning of ejection. These changes are much more pronounced in the ascending than in the descending aorta. If the regurgitation is not severe, the aortic wave approaches closely to normal.

Tracing 5 of Fig. 17 shows the aortic and ventricular waves of a case of well-marked aortic stenosis (blood pressure 80/60). The waves are in striking contrast to those seen in aortic insufficiency. The outthrust of the aortic wave is very slow and gradual, with attainment of a late peak because of the reduced rate of ejection. The systolic limb of the ventricular wave likewise is slower than normal, and the amplitude of the ventricular wave is considerably less than in aortic insufficiency. Katz, Ralli, and Cheer,[8] using intraventricular and aortic pressure curves, in experimentally produced aortic stenosis, have similarly demonstrated a reduced rate of systolic discharge.

The kymographic wave of the pulmonary artery is the only means available at present for recording the pulmonary arterial pulse wave. The wave resembles the aortic wave in all essential details. The incisura is more prominent than in the descending aorta.

Comparison of aortic and pulmonary arterial waves affords a method for studying asynchronism in the ejection phases of the two ventricles, the time of ejection being estimated from the beginning expansion of the vessel to the depth of the incisura. Because of the delay in transmission of the pulse wave from ascending to descending aorta, only the

ascending aorta can be compared with the pulmonary artery in recording the onset of ejection. Wolforth and Margolies[18] have recently similarly studied asynchronism in onset of ejection roentgenkymographically in bundle-branch block but recorded the aortic pulse at the aortic knob assuming a time delay of 0.010 to 0.015 sec. from the ascending aorta.

Table I shows the times of onset and duration of ejection of right and left ventricles in thirty normal individuals. It appears from these

TABLE I

ASYNCHRONISM IN ONSET AND DURATION OF EJECTION OF LEFT AND RIGHT VENTRICLES, ESTIMATED FROM ASCENDING AORTIC AND PULMONARY ARTERIAL PULSE WAVES

	TIME OF ONSET OF EJECTION (SEC.) (FROM START OF RECORD)	DURATION OF EJECTION (SEC.)		TIME OF ONSET OF EJECTION (SEC.)	DURATION OF EJECTION (SEC.)
1. Aorta	0.28	0.24	16.	0.06	0.23
P. A.*	0.30	0.26		0.11	0.25
2. Aorta		0.21	17.	0.25	0.23
P. A.		0.24		0.29	0.21
3. Aorta		0.25	18.	0.34	0.23
P. A.		0.26		0.37	0.21
4. Aorta		0.22	19.	0.33	0.18
P. A.		0.26		0.33	0.19
5. Aorta	0.67	0.19	20.		0.27
P. A.	0.70	0.20			0.26
6. Aorta	0.54	0.20	21.	0.12	0.25
P. A.	0.57	0.23		0.15	0.23
7. Aorta	0.38	0.21	22.	0.52	0.21
P. A.	0.40	0.21		0.51	0.24
8. Aorta	0.18		23.	0.19	0.17
P. A.	0.22			0.22	0.18
9. Aorta	0.20	0.18	24.	0.66	0.19
P. A.	0.23	0.18		0.71	0.19
10. Aorta	0.29		25.	0.67	
P. A.	0.34			0.70	
11. Aorta	0.83		26.	0.48	0.22
P. A.	0.89			0.53	0.23
12. Aorta	0.92		27.	0.15	0.21
P. A.	0.94			0.21	0.25
13. Aorta	0.20	0.26	28.	0.16	
P. A.	0.22	0.24		0.21	
14. Aorta	0.43	0.25	29.	0.53	0.23
P. A.	0.47	0.24		0.55	0.27
15. Aorta	0.40	0.20	30.	0.56	0.18
P. A.	0.42	0.19		0.52	0.24

*P. A., pulmonary artery.

records that neither the onset nor the duration of ejection of the two ventricles is necessarily simultaneous. The duration of ejection was the same in eleven out of twenty-four cases, within the limits of precision (0.02 sec.). In the remaining thirteen the duration of ejection was longer in the right ventricle in nine and in the left ventricle in four. In all four of these cases the left ventricle outlasted the right by 0.02 sec. The right ventricle outlasted the left by 0.02 sec. in two cases, 0.03 sec. in three cases, 0.04 sec. in three cases and 0.06 sec. in one case.

Katz,[9] in an experimental study of asynchronism in dogs, likewise found the right ventricular systole to outlast the left in the majority of cases. The range of variability in his series was 0.04 sec. for those cases of greater duration of left ventricular ejection and 0.07 sec. for cases with greater duration of right ventricular ejection.

In contrast, however, to the inconstant relation in precedence of ejection, reported by Katz, the kymographic studies would show that the onset of ejection regularly occurs earlier in the left than in the right ventricle. In none of twenty-eight cases analyzed did right ventricular ejection precede left, and in twenty-six the onset of ejection

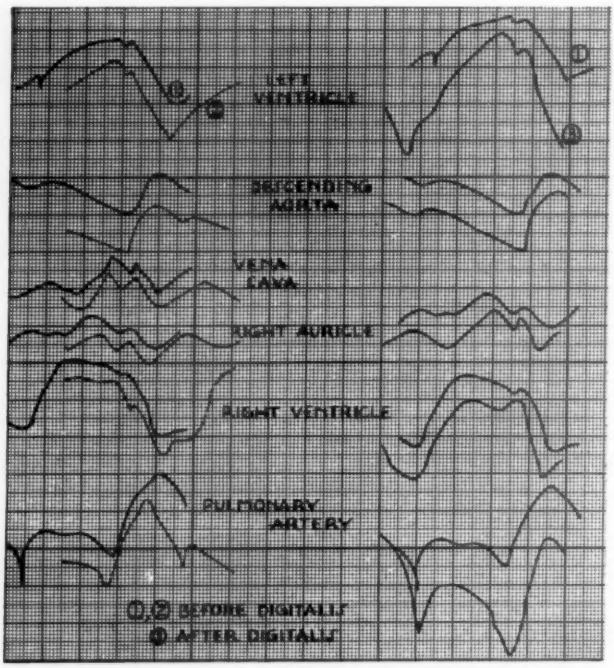


Fig. 18.—Kymographic waves in a normal heart before (*1 and 2*), and twenty-four hours after (*3*), digitalization. The waves at the left represent the movement of the various chambers before digitalis, in two examinations, one day apart, of the same subject. At the right, the lower wave (*3*) represents the movement of the chambers twenty-four hours after digitalis. Wave *1*, the normal, is repeated for comparison.

occurred earlier in the left ventricle, ranging from 0.02 to 0.06 sec. and averaging 0.035 sec. If the onset of the contractile process is simultaneous in both ventricles, this priority of left ventricular ejection can only mean that the isometric, or presphygmic, period of systole is shorter for the left than for the right ventricle. Apparently the greater mass of left ventricular musculature more than compensates for the greater pressure that must be attained isometrically in the left ventricle before the opening of the semilunar valves and onset of ejection.

The effect of digitalization on the duration of ejection and the amplitude of motion of the kymographic waves in four normal hearts is summarized in Table II. No consistent effect was noted. Stewart and Cohn[13] found a reduction of 9 per cent in cardiac area, in investigating the effect of digitalis on normal hearts, and a decrease in systolic output, varying from 8 per cent to 30 per cent and averaging 20 per cent,

TABLE II

EFFECT OF DIGITALIS ON AMPLITUDE OF KYMOGRAPHIC WAVES AND ON DURATION OF EJECTION IN FOUR NORMAL HEARTS

	AMPLITUDE				DURATION OF EJECTION (SEC.)	
	L. VENT.	DESC. AORTA	R. VENT.	PUL. ARTERY	DESC. AORTA	PUL. ARTERY
		mm. × 4				
Bat.						
Control 1	5.3 mm.	15	12	14	0.24	0.27
Control 2	6.0	16	16	17	0.24	0.27
Digitalis—						
24 hr.	6.0	24	17	20	0.24	0.26
48 hr.	5.9	17	--	20	0.22	0.25
120 hr.	5.6	14	15	18	0.28	0.25
DeG.						
Control 1	4.5	10	11(?)	21	0.22	0.22
Control 2	4.5	10	12(?)	14	--	--
Digitalis—						
24 hr.	3.3	12	--	20	0.22	0.19
48 hr.	3.7	10	--	13	0.21	0.21
120 hr.	--	16	--	19	0.22	0.24
Rose						
Control 1	6.6	14	--	19	0.20	0.24
Control 2	5.5	14	14	--	--	--
Digitalis—						
24 hr.	6.9	16	16(?)	19	0.23	0.28
48 hr.	6.0	12	21	18	--	--
120 hr.	6.8	14	17	30(?)	0.23	0.27
Gre.						
Control 1	4.7	11	20	30	--	--
Control 2	4.7	12	24	24	0.26	0.38
Digitalis—						
24 hr.	5.8	16	22	32	--	0.32
48 hr.	5.8	14	21	26	--	(about) 0.36
120 hr.	6.1	14	20	27	0.27	0.27

determined by the acetylene method. The heart rate was slowed from four to fourteen beats. The maximum effects were obtained within twenty-four hours. Apparently these changes are not associated with any significant alteration in cardiac movement. Fig. 18 shows a graphic record of one of these cases. These tracings illustrate, also, the constancy of the kymographic waves in the same subject at different times.

SUMMARY

Roentgenkymography records the movements of the heart and great vessels and is to be included among the methods of graphic registration of the cardiac cycle in man.

All the phenomena recorded kymographically conform readily to physiological interpretation, the information afforded by the ventricular, aortic, and auricular waves being the same as is obtained experimentally with the myocardiograph, arterial sphygmograms and jugular pulse tracings, respectively. On the basis of correlation with the electrocardiograms and heart sounds, the waves may be assigned to specific events in the cardiac cycle, and, by correlating these waves graphically, the sequence of events in the cardiac cycle may be accurately studied, with a time resolution of 0.02 sec.

The findings serve in the main to corroborate relationships determined by animal investigations. The kymographic method, in addition, sheds light on a number of interesting aspects of the cardiac cycle. Thus, it is the only method available for obtaining in man a graphic registration of occurrences in the pulmonary circuit.

Asynchronism in ejection of the two ventricles is studied by comparing aortic and pulmonary artery waves.

Physiological aortic regurgitation is demonstrated.

The changes in mitral and aortic valvular disease are shown, and a dynamic interpretation of these changes is given.

The effect of digitalization on the duration of ejection and movement is considered.

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THE RELATIONSHIP OF TACHYCARDIA TO CARDIAC INSUFFICIENCY*†

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IN EXPLAINING the common association of tachycardia with cardiac insufficiency, the acceleration usually has been regarded as a cause of the insufficiency. Although this explanation now is applied more especially to cases with auricular fibrillation, before recent data referring congestive heart failure to other causes became available, it was employed quite generally. Usually no particular explanation of the acceleration itself has been offered. Whether or not there is valid ground for the assumption that fast beating causes heart failure, however, there is indubitable evidence to show that myocardial failure is a prominent cause of acceleration.

REFLEX ADJUSTMENT OF SINUS RATE TO OTHER FACTORS IN THE CIRCULATION

It is known that the various factors in the circulation tend to be maintained in proper balance by reflex adjustments. Primary change in ventricular rate tends to bring compensatory change in the systolic discharge and in blood pressure. Conversely, primary change in blood pressure, from variation in the arterial bed or in ventricular output, produces reciprocal effect in sinus rate.

Under the title, "Physiologic Meaning of Common Clinical Signs and Symptoms in Cardiovascular Disease," Wiggers[1] says that "when arterial pressures fall, due to primary vasodilatation or to diminished cardiac output, the heart accelerates and strives to restore arterial pressures to normal." He reminds us of the pathways involved in this reflex acceleration, one over the afferent branches of the vagus from the root of the aorta, and the other through the so-called sinus nerve which is distributed solely to the carotid sinus, a reflex pathway exhaustively studied by Weiss and Baker.[2]

Tachycardia in Peripheral Circulatory Insufficiency.—It is beginning to be appreciated that this reflex mechanism is responsible for the tachycardia that usually accompanies failure of the peripheral circulation. In a recent publication Warfield[3] directs timely attention to this fact and reminds us that in such circumstances therapeutic effort must be

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†Read before the American Heart Association, May 12, 1936.

directed not toward slowing the heart but toward improvement of the adverse factors in the peripheral circulation, of which tachycardia is but a physiological result.

Tachycardia in Circulatory Insufficiency of Cardiac Origin.—The same physiological response in heart rate is brought about also in cases of circulatory failure with normal rhythm in which the heart rather than the arterial bed is primarily at fault. The matter is expressed clearly by Wiggers:

> The . . . compensatory type of cardiac acceleration is produced through these reflex mechanisms not only when peripheral vasodilatation exists but also when the systolic discharge of the heart is reduced. Shock and hemorrhage are two clinical conditions in which such a reduced output and compensatory acceleration obtain. But it is not so generally appreciated that the same reflex mechanisms operate when ventricular discharge is reduced as a result of myocardial failure and that the tachycardia which is so characteristically present is nature's only method of maintaining an effective circulation.

With the acceleration which nature institutes in a failing circulation, both phases of the cardiac cycle are shortened; and, as Lewis has emphasized, the lessening of the diastolic phase is proportionately greater than that of the phase of systole. The rest period is curtailed. Other circumstances also bear upon the work of the muscle. It receives less blood to expel. With each beat its work is less. Whether fast or slow, however, with each contraction it uses up its energy and then accumulates another supply. The term "cardiac reserve" applies not to a holding back in systole but to an ability to increase its use of available energy. One of its very means of putting its reserve capacity into use when called for is by acceleration—not a harmful but a useful process. With a rate too high for proper adjustment, diminution in output may embarrass the general circulation, but damage applies primarily not to the heart. This compensatory acceleration is described by Wiggers as follows:

> Dynamic studies have shown that the faster the heart beats, the more the period of diastolic filling is cut short and the more the systolic discharge is decreased. However, calculations show that this decrease is more than compensated by the cardiac rate, up to 200 per minute, so that the minute output steadily becomes greater.
>
> It is obvious that this this compensatory acceleration must not be disturbed. To do so would cause a drop in blood pressure sufficient, perhaps, to endanger life itself. Fortunately there is no medicinal agent by which a compensatory sinus tachycardia can easily be abolished; otherwise many a patient with serious heart disease would have been helped prematurely to his grave through kindly intentioned but misguided treatment.

HEART FAILURE AND THE THERAPEUTIC ACTION OF DIGITALIS

Wiggers' statement concerning misdirected attempts primarily to slow compensatory sinus tachycardia applies particularly to former notions of the harmful effects of acceleration upon the heart and to the use of digitalis primarily to reduce it.

More recent investigations relate heart failure not to the using of its available energy but to agents which impair the ability of the muscle to do that very thing. Infection, strain, and diminished blood supply particularly are involved. Such agents lessen the efficiency of the muscle by causing it to be less economical in transforming energy into work. It is now recognized that in congestive heart failure the efficiency of the ventricle is improved by the direct action of digitalis upon the muscle. Greater economy results. In a recent publication of great importance, Peters and Visscher[9] report their studies on "The Energy Metabolism of the Heart in Failure and the Influence of Drugs Upon It." They say:

> Our main object in the study of the digitalis series of glucosides has been to determine whether they do or do not increase the efficiency with which the heart muscle is able to perform work. In every instance, among the clinically useful glucosides employed, there was an unmistakable increase in efficiency. . . . These drugs make the heart more economical in its utilization of energy and are therefore conservative in their effect.

The Relationship of the Effect of Digitalis to Sinus Slowing.—This therapeutic effect of digitalis directly upon the muscle of the ventricle, questioned by Mackenzie, was denied by Sir Thomas Lewis. Lewis insisted that the favorable action of the drug was to be attributed solely to its ability to reduce ventricular rate—a result obtained only in cases of auricular fibrillation. Sutherland and others, however, observing benefit in normal rhythm cases, administered the drug in normal rhythm also, with the object of slowing the rate.

Accumulated evidence that in congestive heart failure digitalis possesses a beneficial action unrelated to slowing finally became conclusive. It is known now that this action of the drug is exerted directly on the ventricular muscle. In normal rhythm cases, moreover, authorities now agree that improvement is due to this muscular action alone. They find that therapeutic doses produce little direct effect at the pacemaker but that, in cases with acceleration, slowing is an indirect effect which follows the improvement in the circulation produced by the action of digitalis upon the muscle of the ventricle.[4, 5, 6, 7, 8] With better circulation physiological mechanisms produce a reciprocal adaptation of rate. Tachycardia subsides. Just as acceleration results from impairment, so slowing results from improvement. Both are im-

portant indices of circulatory efficiency. Tachycardia may suggest that the circulation needs help; slowing indicates that appropriate measures have been effective.

In cardiac insufficiency with normal sinus rhythm, acceleration is not the cause of the failure; it is a physiological result. Primary slowing is not a proper therapeutic objective and is not a direct effect of digitalis. Improvement in muscular efficiency by digitalis or other agents results in subsequent slowing—a reflex adjustment in rate.

TACHYCARDIAS OF ABNORMAL RHYTHMS

With regard to abnormal rhythms it is evident that neither in origin nor in abatement do they represent compensatory adjustment of rate to other circulatory influences. Adaptation in other components of the circulation must be made, if possible, to meet the rate of the ectopic rhythm. As noted above, with sinus rates up to about 200 per minute, the circulation remains adequate, but in certain abnormal rhythms special factors obtain.

A. Auricular Flutter.—In auricular flutter the efficiency of the ventricular beat is lessened in some degree by the absence of auricular systole. Authorities differ somewhat regarding the extent of the circulatory impairment so produced. In the unusual instances of 1 to 1 ventricular response, the rate of the ventricle exceeds the upper limit at which compensatory adaptation in output can be accomplished. Blood pressure falls. The circulation is inadequate, and measures designed primarily to abolish the abnormal tachycardia may become in order.

B. Independent Ventricular Rhythms.—In ventricular tachycardia also the ventricle is deprived of the mechanical advantage of a preceding auricular systole. The rate usually is at about the upper limit at which adequate circulation can be maintained. In some cases the tachycardia itself thus may be a handicap, but a circumstance of much greater significance regularly obtains. The ectopic origin of the stimuli causes the muscular elements to be activated in abnormal sequence. The resulting contractions of the ventricular segments are much less efficient in expelling blood than is the concerted arrangement of normal systole. It is chiefly to this abnormal sequence of muscular contraction rather than to the high rate of beating or to the failure of auricular aid that circulatory insufficiency is to be attributed.[1] Primary efforts in such cases properly may be directed toward the restoration of normal rhythm.

C. Auricular Fibrillation.—In auricular fibrillation the excitatory impulses flow into the ventricular segments along normal paths; systole thus is spared the embarrassment that applies to independent ventricu-

lar rhythms. It is, however, deprived of the help normally supplied by auricular systole. In most clinical cases of fibrillation the minute rate of the ventricle is well below the critical physiological limit. But in many instances the fractional rate is too high, so that in cases with great acceleration the tachycardia itself may be somewhat disadvantageous with respect to optimum circulation. Certainly it would be desirable to abolish such an abnormal rhythm however slight might be its adverse circulatory effects, provided its cessation could be accomplished with reasonable prospect of permanence, and with minimum danger. The history of the disappointing use of quinidine in unselected cases of fibrillation need not be recited. In cases of heart failure with auricular fibrillation it is seldom possible to maintain normal rhythm by quinidine or other means.

As an alternative procedure, a proper reduction of ventricular rate in cases with excessive tachycardia obviously would be desirable for the general circulation. But in the average case with acceleration of lesser degree, less advantage would appear to accrue from primary reduction in rate, even if possible of accomplishment. For a long time, however, digitalis has been employed primarily with this objective. More recent information of the causes of heart failure and of the therapeutic action of the drug, and later data regarding the origin of fibrillation itself, now appear to necessitate a reexamination of this time-honored use of digitalis.

The Origin of Auricular Fibrillation.—Contrary to Lewis's dictum that persistent fibrillation means disease of the ventricular muscle, authorities now realize that no such interpretation is warranted.[10, 11, 12] In a recent study of 431 consecutive cases of the arrhythmia from the records of the Barnes Hospital, Dr. E. O. Jeffreys and I[13] found no suspicion of ventricular disease in forty-two cases. Auricular fibrillation is to be referred to the auricle. As precipitating factors, nervous influences and toxic agents have long been recognized. Later studies of the origin of clinical auricular fibrillation strongly suggest that in many instances a prominent precipitating factor is increase in intra-auricular pressure. In our series Dr. Jeffreys and I noted the usual findings, that mitral valve lesions were present in about one-third of the cases and that congestive heart failure was present in about two-thirds.

That stretching of the auricular wall from the increased pressure of congestive heart failure is a frequent factor in the origin of fibrillation is no new conception. It is supported by experimental data and by a rapidly increasing amount of clinical evidence. Congestive heart failure is so common a precipitating factor that, in any case in

which no other cause appears more probable, it should be suspected. In the excellent study recently made by Nahum and Hoff[14] those authors say:

> When heart failure with auricular distention and venous engorgement occurs, the stretch of the auricle may contribute the necessary stimulus (E) which, when in association with vagus overactivity, precipitates auricular fibrillation. It thus becomes clear why this irregularity is so often associated with heart failure, being rightly regarded as an important evidence of the existence of heart failure.

All in all, in the average case of congestive failure and auricular fibrillation the probability increases that it is not the fibrillation which has caused the failure, but the failure which has caused the fibrillation. In many cases of heart failure observed over a period of time, the fibrillation is known to be secondary.

Differentiation of Cases With Regard to the Slowing Effect of Digitalis.—It is significant that in toxic cases of auricular fibrillation without heart failure, digitalis produces no slowing. In his classic treatise (1910), Mackenzie[19] said:

> Moreover, when the heart is affected by agents which increase its excitability, the digitalis has little effect upon the rate, whether there is auricular fibrillation or whether the rhythm is normal. . . . This failure of effect is also evident in conditions where the heart is affected by poisons. . . . A modification in the susceptibility to digitalis is also produced by certain changes in the cardiac muscle.

Although the experience of physicians generally has made them aware of this fact, they appear more or less to have disregarded it.

Still another fact of perhaps greater import appears not to have been so generally appreciated. Not only in toxic cases but regularly in cases of fibrillation unassociated with heart failure, the therapeutic administration of digitalis is without slowing effect. We divided our cases on the basis of congestive heart failure. In the group without heart failure were put only cases in which there was no suspicion of failure. There were 97 in this group. In 47 of these cases without heart failure digitalis was administered, but in no instance did the record give evidence of a slowing effect on the pulse. It is possible, of course, that upon some occasion pulse records might have failed to reflect ventricular slowing, but it is extremely improbable that this could have obtained in many instances.

Determination of Rate.—In auricular fibrillation the ventricular rate is determined by the number of fibrillary impulses which evoke contractions of the muscle. Impulses which are not followed by contractions either fail to reach the ventricle, or, reaching it, find it unresponsive. In clinical explanations of any failure of ventricular response, it has been customary to give consideration to conductivity but to leave altogether out of account the matter of ventricular excita-

bility. Physiological investigation, however, finds the matter not so simple. Erlanger[15] holds that certain stimuli may reach the ventricle but find it unresponsive. He gives consideration to diminished excitability as an important factor in so-called A-V block. In normal rhythm, the P-R interval measures the time elapsing between the beginning of auricular activity and the recorded beginning of ventricular response. It cannot be regarded as a measurement of transmission time alone. The degree of ventricular excitability may be a factor as truly as the degree of conductivity. Sharp differentiation, in fact, between the ultimate fibers of the bundle and the rest of the musculature is impossible. They become an indistinguishable whole. Physiological evidence is to the effect that excitability and conductivity vary together.

It is known that as the ventricular rate falls irritability increases,[16, 17, 18] and that with improvement it diminishes again. Many years ago Cushny and his coworkers[17] took this fact into account in explaining the slowing effect of digitalis in cases of heart failure with fibrillation. In congestive failure digitalis appears to lessen both conductivity and irritability, if indeed they can be regarded as separate properties. At least it is known to lessen ventricular irritability,[18] which is more readily susceptible of separate measurement. It is significant that in fibrillation digitalis slowing occurs only in cases of heart failure, i.e., under circumstances in which muscular improvement regularly follows from the direct action of the drug, an effect which renders the muscle less susceptible to smaller fibrillary stimuli.

In explaining the block-producing effect of digitalis, attention has been centered too much on the A-V tissues, too little on the muscle of the ventricle. In the light of the demonstrated effect of the drug on the musculature, it appears illogical not to take this action prominently into account in explaining the lessening of ventricular response from digitalis in cases of auricular fibrillation with heart failure.

SUMMARY

The various elements of the circulation are subject to reflex variation. By reciprocal adjustments balance tends to be maintained despite disorder in one component.

Primary impairment of the peripheral circulation or of cardiac output produces reflex acceleration of sinus heart rate. Compensatory tachycardia is physiological, not harmful. Its primary abatement is not a proper therapeutic objective. Improvement is followed by reverse slowing. Conversely, primary acceleration of rate tends to induce compensatory adjustment in blood pressure, and in systolic discharge. With sinus rates nearly as high as 200, the circulation remains adequate.

Abnormal rhythms are not subject to reflex compensatory adjustment in rate. Certain special features, also, may affect the circulation adversely.

In auricular fibrillation the ventricular rate appears to depend largely upon the state of the ventricular muscle. This arrhythmia frequently occurs in congestive heart failure. Under such circumstances reduction in rate follows improvement in the muscle, from digitalis or from other cause. In cases of fibrillation without heart failure the muscular effect of digitalis is not beneficial; in such instances administration of the drug is not followed by slowing. In auricular fibrillation, as in normal rhythm, abatement of tachycardia appears not to be the cause of improvement but to be the result of it.

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THE DIFFERENTIAL DIAGNOSIS OF CONGESTIVE HEART FAILURE AND CONSTRICTIVE PERICARDITIS (PICK'S DISEASE)*

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IN A symposium on cardiac insufficiency it seems appropriate that there be included a description of an important syndrome that produces a picture in many respects similar to that of congestive failure but in which the mechanism is entirely different and not dependent upon the failure of the heart as a pump. This syndrome is the one due to acute, subacute, and chronic constrictive pericarditis.

It is important that this be done for the reason that the therapy may be quite different from that of congestive failure and the prognosis, in suitable cases, is infinitely better. This lies in the fact that there is a specific treatment for many of these patients, namely, paracentesis in acute cases, and resection of the constricting pericardium in chronic cases, with marked or almost complete relief of symptoms in a large number.

In acute or subacute pericardial inflammation with more or less rapid accumulation of effusion, the effects on the circulation are the results of cardiac tamponade, the collection of fluid—serous, sanguineous, or purulent—compressing the heart and preventing its dilatation to receive the blood. In this syndrome all the signs may arise rapidly, and the patient appear to be suffering from marked peripheral venous distention and enlarged liver combined with the signs of much diminished cardiac output. The accumulated fluid may increase the cardiac dullness considerably, but cardiac tamponade becomes extreme only when the stretching of the pericardium is unable to compensate for the reduced diastolic volume of the heart. Such an event occurs in malignant or purulent pericarditis, either metastatic or from direct extension, in some cases of tuberculous effusion, rarely in rheumatic pericarditis, in cases of aneurysm rupturing into the pericardium, or rupture of the heart wall after coronary occlusion, and most characteristically in injuries to the heart from gunshot or stab wounds. In such cases the therapeutic indication is clearly not the reduction of the compensatory venous hypertension by venesection but the relief of the pressure on the heart by paracentesis of the pericardium or by surgical exploration

*Read before the American Heart Association, May 12, 1936.

and drainage. By repeated tapping some cases of inflammatory effusion may be helped to subside to such a stage of chronicity that pericardial resection may be feasible.

There still exists in the minds of many physicians the belief that the diagnosis of chronic constrictive pericarditis is almost impossible and that there is little to be gained from it except a sense of diagnostic satisfaction on the part of the doctor. This belief originates in a confusion between the various types of pericardial disease, some of which merely complicate the pathology of an otherwise badly diseased heart in which the discovery of a concomitant pericardial involvement has little bearing upon treatment or prognosis. This is true in the case of the commonest example of pericardial inflammation—that due to the pancarditis of rheumatic infection. In this condition the myocardium and the heart valves are, so far as we can prove, almost universally involved. In sixty-two cases of acute rheumatic pericarditis studied at the House of the Good Samaritan in Boston for periods up to ten years after the acute attack, there were only two cases which showed no clinical evidence of valvular deformity.[1] In such cases it is clear that the knowledge that an adherent pericardium exists, as assumed from the history of the acute attack, adds nothing to the therapeutic or prognostic implications except to reinforce the belief that a severe carditis has occurred, since rheumatic pericarditis, certainly as a part of pancarditis, does not cause Pick's disease so far as is attested by our experience. Furthermore, when patients with rheumatic heart disease suffer from congestive failure, the degree of this that is attributable to a complicating adherent pericardium cannot be differentiated from that due to the myocardial insufficiency. Completely adherent pericardium of itself is frequently an unimportant finding and is found in a considerable percentage of routine autopsies—2.26 per cent of the cases in a series of 1,900 autopsies from the Massachusetts General Hospital showed chronic pericarditis of some degree.[1] In most instances these pericardial scars and adhesions represent the historical mementoes of mild infections or perhaps the effects of the benign idiopathic pericarditis that not infrequently occurs and is probably not infrequently missed. It has not been proved that such infections, from which the patient apparently recovers completely, are ever the cause of constrictive pericarditis appearing in later life.

Pick's disease, on the other hand, is a condition that is usually progressive from the time of the original infection, and the inflamed pericardium in passing into a subacute stage or in healing gradually thickens as it enfolds the heart in its inelastic grip. Its etiology is unknown, but in our experience it would appear to arise from a tuberculous infection or from the agent responsible for respiratory infections, such as influenza and pneumonia. Rarely it follows septic pericarditis. Rheumatic infection has been outstandingly absent in our series.

DIAGNOSIS

To arrive at a diagnosis of constrictive pericarditis it is necessary to be very critical of the evidences of congestive failure which are often grouped indiscriminately without reference to the vital distinction between right and left ventricular failure. In pure left ventricular failure the hypertension of the venous circuit predominates in the lungs, while in right ventricular failure it is most marked in the peripheral veins. Artificial as this rigid division may be in many cases of cardiac failure, it is fundamental in the diagnosis of all types of cardiac insufficiency. We may instance as pure left ventricular failure the syndrome of cardiac asthma and acute pulmonary edema in hypertensive heart disease, and as pure right ventricular failure the dilatation of the right heart following complete embolic obstruction of the pulmonary artery. But as a clinical picture in the terminal stages, hypertensive heart disease results in an added strain and hypertrophy of the right heart from the back pressure in the lungs and the development of peripheral edema and increased venous pressure. Similarly, so well marked an example of pure right ventricular failure as that seen in mitral stenosis occurs as a response to the hypertension in the lungs from the obstruction at the mitral valve so that there is increased venous pressure in both greater and lesser circuits.

These examples are what the "Criteria for the Classification and Diagnosis of Heart Disease," approved by the American Heart Association, describes as instances of cardiac insufficiency or "failure of the heart as a pump." This implies failure of the heart to empty itself in the sense of a force pump. In the case of Pick's disease there is primarily a failure of the heart to fill itself, or with the previous analogy, it can only be called "failure of the heart as a pump" if the heart is thought of as a suction pump. A rather similar condition actually exists in mitral stenosis in which the emphasis of venous engorgement presents itself in the pulmonary circuit due to inability of the left ventricle to fill properly through the stenosed mitral valve. Disregarding the eventual defeat of the right ventricle with its failure to empty, one sees a small left ventricle discharging into the aorta all that it receives, and it is no more to be blamed for the ineffectiveness of the arterial circulation than is the whole heart in Pick's disease.

By such analogies we arrive at the essential physiology of constrictive pericarditis in which the heart chambers are fundamentally normal but in which the blood is prevented from entering them either by adhesions about the exits of the venae cavae, or more often by the fact that the chambers are hindered in their capacity to dilate and receive the blood because of the inelastic armor of the thickened pericardium. In mitral stenosis the *vis a tergo* helping to force blood through the valve is the

power of the right ventricle, plus the pulmonic hypertension. In concretio cordis there is no mechanism to help fill the heart except the compensatory rise in peripheral venous pressure.

Naturally enough the syndrome of chronic constrictive pericarditis can be simulated by other obstructions to venous inflow of the heart, such as tumors, emboli, or thrombi in the venae cavae or right auricle, or by narrowing of the tricuspid valve. Since tricuspid stenosis is practically never seen without mitral stenosis, this does not enter into the differential diagnosis, provided mitral disease and its attendant pulmonary congestion are evident.

It follows, therefore, that the picture in Pick's disease is one of marked distention of the peripheral veins with either absent or only relatively slight distention of the pulmonic vessels, and the signs and symptoms are in accord. The chief points are these:

1. The patient is usually a child or young adult.

2. Ascites and enlarged liver appearing insidiously are always present and usually out of proportion to the peripheral edema.

3. The veins in the neck are engorged, and the venous pressure in arms and legs is often over three times normal. Moreover, the venous pressure remains constantly elevated, not fluctuating through periods of improvement or regression as it does in congestive heart failure. (The ascites alone may increase the femoral venous pressure considerably, and the pressure will be reduced somewhat by abdominal paracentesis.)

4. Dyspnea may be present to some degree on exertion, but orthopnea is strikingly absent when there is no pleural fluid.

5. Cyanosis consistent with venous engorgement is present and may be intense. When combined with lack of orthopnea and marked ascites, the inconsistency of these signs, at first suggesting congestive failure, is striking. Only marked tricuspid stenosis and pulmonary heart disease simulate it.

6. The heart size is normal in most cases—seven out of fifteen in the Massachusetts General Hospital series (moderate enlargement occurred in only three).[2]

7. The heart is free from murmurs except for infrequent apical systolic bruits. The rhythm is usually normal, but auricular fibrillation occurred in four of White's fifteen cases.

8. The blood pressure and pulse pressure are low. "Paradoxical pulse" was present in seven, absent in two, and not noted in six of the Massachusetts General Hospital series.

9. Broadbent's sign is absent.

10. Pleural effusions are common.

11. X-ray pictures of the heart may show calcification of the pericardium, limitation of cardiac pulsation, or limitation of pulsation of

the right border, dilatation of the superior vena cava, dilatation of the auricles, prominence of the left upper border, and pleural thickening. However, the examination may be essentially negative.

12. Electrocardiography shows low voltage in the axial leads, or inversion of the T-waves in Leads I and II, of the coronary type. One or both of these findings occurred in all of the fourteen Massachusetts General Hospital cases electrocardiographed.

13. The differential diagnoses of importance in our experience have been those of congestive heart failure (especially with mitral stenosis), cirrhosis of the liver, polyserositis, and nutritional edema.

SUMMARY

Acute and chronic constrictive pericarditis cause signs and symptoms suggestive of cardiac insufficiency (congestive failure) but should not be mistaken for it since paracentesis or the surgical relief of the chronic condition may result in complete disappearance of the patient's disability.

The diagnosis is made by noting, usually in a young person, the inconsistency between the finding of cyanosis, persistent venous distention, ascites, edema, and enlarged liver on one hand, and the absence of orthopnea, cardiac enlargement, and signs of valvular disease on the other. Helpful further evidence can be found in the low blood and pulse pressure, paradoxical pulse, limited cardiac excursion or calcification of the pericardium by x-ray, and low voltage or T-wave inversions in the electrocardiogram.

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A CASE OF CONGENITAL AORTIC ATRESIA*

With Hypoplasia of Ascending Aorta, Normal Origin of Coronary Arteries, Left Ventricular Hypoplasia and Mitral Stenosis

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AN EXTREME form of morbus ceruleus, which terminates fatally usually during the first few days of life, is associated with closure of the aortic or mitral valvular orifices. Cases of stenosis of these orifices, congenital or acquired, are not uncommon, but complete atresia of either passage is one of the very rarest types of congenital heart disease. Especially is this true of aortic atresia. The present case is accordingly reported, together with a survey of the previously described instances, which collectively point to the suggestion that the size of the interatrial aperture is a factor influencing the duration of life.†

CASE REPORT

The subject was a colored male infant, the firstborn of twins. The mother (G. J.) was a negro girl, aged nineteen years, married one year, primigravida. She was first examined Oct. 30, 1934, when the last menstrual period was stated to have been in May, 1934. Wassermann test was negative. She was seen at intervals in the Charity Hospital Out-Patient Clinic until admission to the obstetrical ward of the Charity Hospital on January 14, 1935. No significant findings were discovered in her past or obstetrical history, or on physical examination. Pelvis of normal type. Fetal heart tones were heard to the left of the umbilicus, at a rate of 140 per minute. The first stage of labor began at 3:00 P.M., Jan. 14, 1935, the second stage at 4:30 A.M., Jan. 15, 1935, when the membranes were ruptured artificially. A frank breech, S. L. A., was delivered at 4:35 A.M.; the child breathed instantly and cried vigorously. At 4:50 A.M. the second child, vertex presentation, L. O. A., was delivered without difficulty; after two gasps this infant stopped breathing. Resuscitation was attempted for forty minutes, with the child taking occasional gasps at first; carbon dioxide, mouth-to-mouth breathing, alphalobelin, caffeine, contrast baths, and warmth all failed, and at 5:30 A.M. this second child was pronounced dead. Both were males. Their weights were, respectively, 6 pounds, 3 ounces, and 5 pounds, 6 ounces. The afterbirth was described as "one placenta, two cords, two sets of membranes."

The first child (the case here reported) died at the age of 20½ hours. When born he seemed to have neither cyanosis nor dyspnea, but very shortly thereafter cyanosis became apparent, and in the course of several hours there was also marked dyspnea. The cyanosis continued to deepen rapidly, and just before death both cyanosis and dyspnea were extreme.

Autopsy.—Negro male, body length, 47 cm. Second degree lividity of skin. Hair normal in amount and distribution. Nose showed a depressed bridge. Head

*From the Department of Anatomy, the Tulane University of Louisiana School of Medicine.

†The writer is indebted to the Department of Pathology (Dr. Joseph Rigney D'Aunoy, director), the Charity Hospital of Louisiana, for the specimen here described.

showed loose suture lines, with evidence of craniotabes. Blood in mouth. Mesenteric vessels were somewhat engorged with blood, especially on the venous side. Lungs were almost completely atelectatic in the two upper lobes, and completely atelectatic in the three remaining lobes. They were about the color of liver, firm and rubbery in consistency. Very little crepitation was present. Liver weighed 105 gm. and capsule was tense; cut surface presented the appearance of a nutmeg liver. Spleen weighed 7 gm. and cut surface showed a little hyperemia and congestion. Kidneys

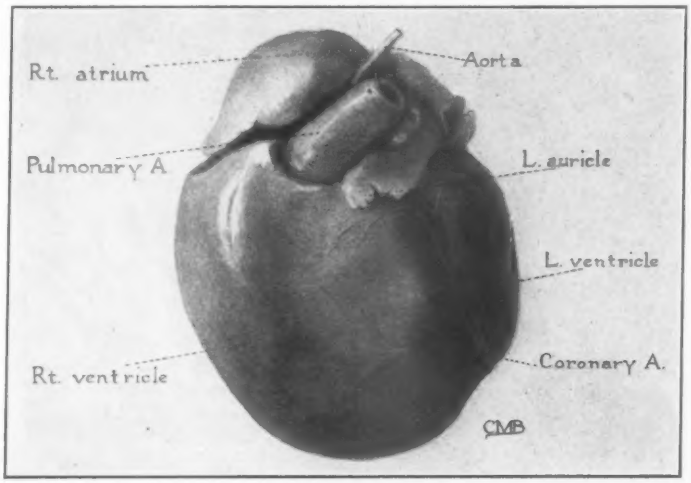

Fig. 1.—Anterior surface of heart.

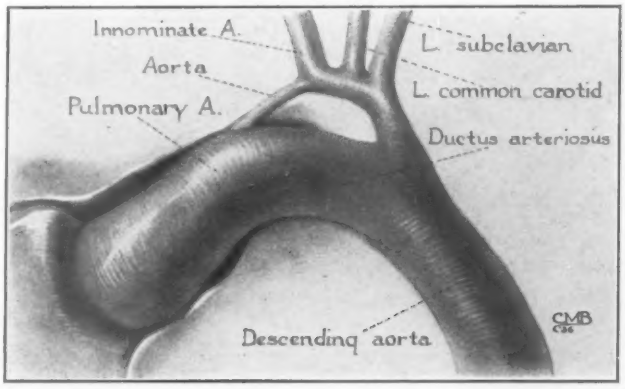

Fig. 2.—Vessels at base of heart, showing disproportion between pulmonary artery and aorta and manner by which blood from the ductus arteriosus reaches the ascending aorta, the vessels of the neck, and the descending aorta. (Functionally a "truncus solitarius pulmonalis.")

were congested, capsule tense, and cut edges everted on sectioning; they were red, with much uric acid deposition. Brain showed slightly engorged blood vessels. On sectioning, the epiphyses exhibited normal ossification centers and appeared perfectly normal.

Microscopical Examination: The *spleen* showed no increase in interstitial tissue, but the sinusoids were markedly engorged, and the pulp showed reduction in number of cells; corpuscles were numerous, small, but well defined. In the *liver* the

sinusoids of central portions of lobules were much engorged. Parenchymal cells in periphery of lobules showed rather marked fatty degeneration, and many islands of blood-forming tissue were found. In the *lung* the vessels were markedly engorged; a few of the alveoli were overdistended, but the majority were completely collapsed or only partially distended with air. *Kidney* except for congestion showed no morbid change. No other developmental abnormalities were seen except those of the heart, to be described in detail below.

Anatomical Diagnosis.—Congenital cardiac anomaly. Atelectasis of lungs. Marked congestion in liver, spleen, kidneys, brain and lungs.

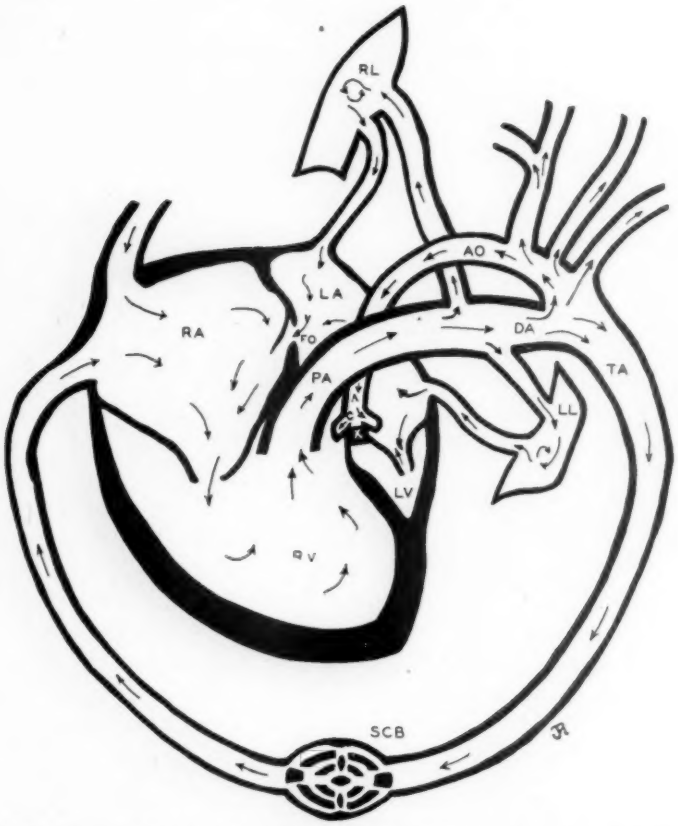

Fig. 3.—Diagram of the heart chambers and vessels, to show the probable course of the blood. (For clearness, no attempt is made to retain proportions here.) *AO*, arch of aorta; *A*, aorta ascendens; *C*, right and left coronary arteries; *DA*, ductus arteriosus; *FO*, foramen ovale; *LA*, left atrium; *LL*, left lung; *LV*, left ventricle; *PA*, pulmonary artery; *RA*, right atrium; *RL*, right lung; *RV*, right ventricle; *SCB*, systemic capillary bed; *TA*, descending thoracic aorta; *X*, septum causing aortic atresia.

Autopsy on the second twin revealed nothing of significance except atelectasis of lungs and generalized passive congestion. The heart was normal.

Description of Cardiac Anomaly

The heart was approximately normal in general shape, in size (5.4 by 4.1 by 2.9 cm.), and in weight (25 gm.). It appeared well nourished, with no areas of infarction, ischemia, or anemia; the coronary vessels were engorged with blood, especially the veins. There was a great disproportion between right and left ventricles

(Fig. 1); the anterior width of the right ventricle was 3.2 cm., of the left, 0.9 cm. The apex was formed entirely by the right ventricle. The pulmonary artery was tremendously enlarged, being 13 mm. in external diameter at the root. The right and left branches of the pulmonary artery, superior and inferior venae cavae and pulmonary veins were normal. The ductus arteriosus continued in the direct axis of the pulmonary artery and was of the same diameter.

The aorta at once attracted attention. It was threadlike throughout its ascending and arched portions, being 2 mm. in external diameter. Near the isthmus it became slightly larger and gave origin normally to the three great vessels (Fig. 2). Below the isthmus the descending thoracic aorta was the expected diameter, appearing as the continuation of the large ductus arteriosus.

The right atrium was found to be greatly dilated and moderately hypertrophied. It measured 21 by 14 by 19 mm. and its walls were 1 mm. thick. The orifice of the coronary sinus was in its normal position, but much dilated. The right auricle was greatly dilated, appearing to be more directly a part of the atrial chamber than an appendage. On the septal wall was a very large fossa ovale which distinctly

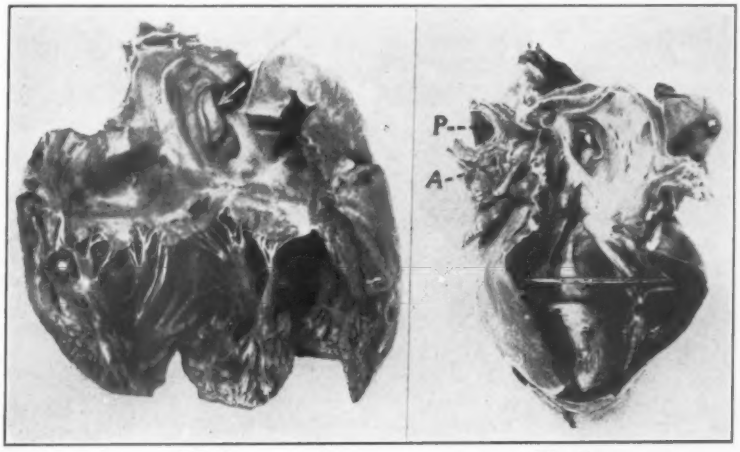

Fig. 4. Fig. 5.

Fig. 4.—Heart opened to show enlargement of the right atrium and ventricle. Arrow indicates abnormal flap of tissue which prevents the flow of blood from right to left.

Fig. 5.—Heart opened to show marked hypoplasia of left atrium and ventricle. Note small opening of foramen ovale. *A*, ascending aorta; *P*, pulmonary artery.

bulged into the left atrium; it was circular, 11 mm. in diameter. The foramen ovale, 3 by 2 mm., was situated in the upper anterior portion of the fossa ovale. This was bounded in front by the prominent edge of the thick septum secundum (concave posteriorly) and behind by the edge of the thin, filmy septum primum. The foramen ovale so formed was in addition guarded by an unusual flaplike fold of tissue (Fig. 4); this bulged toward the *right* atrium, despite the "herniation" of the fossa ovale into the left atrium (Fig. 3). This fold or flap of tissue formed a valve which must have fairly effectively obstructed blood flow from right to left, while at the same time admitting it from left to right.

The tricuspid valve was 14 mm. in diameter; its cusps were normal in relative size and position although each cusp was actually much larger than usual. These cusps were attached as usual to three sets of large papillary muscles by rather massive chordae tendineae. The right ventricle showed marked dilatation and hypertrophy (Fig. 4). Its walls averaged 7 mm. thick, its internal width was

25 mm., depth 14 mm., and height 26 mm. The conus region was much larger than usual, appearing almost as an additional chamber; it opened into the pulmonary artery, which also showed extreme dilatation and hypertrophy. The pulmonary orifice, 9 mm. in diameter, was guarded by three strong, perfectly normal cusps which were in the usual positions. There was no opening in the aortopulmonary septum.

The left atrium (Fig. 5) was found to be less dilated than the right. Its walls were not hypertrophied, being less than 1 mm. thick. It measured 14 by 9 by 7 mm. The auricular appendage was in its usual position, but unlike that on the right was extremely hypoplastic; it joined the atrium by a narrow isthmus 1.5 mm. in diameter.

The left atrioventricular orifice presented a distinctly stenotic valve, tiny, funnel shaped, showing no subdivision into cusps. Its edges were connected by abnormally slender chordae tendineae to the left ventricular walls, with little evidence of papillary muscles. The valve was stenotic, the minimum diameter of the passage being less than 2 mm., while at the level of the fibrous ring it measured 6 mm.; evidently there existed a "mitral atresia" from a functional standpoint. The left ventricle, corresponding to the external indications of its size, was extremely hypoplastic. It was really little more than a slitlike cavity in the wall of the massive right ventricle, and it is thus easy to see why such a heart might be described as a

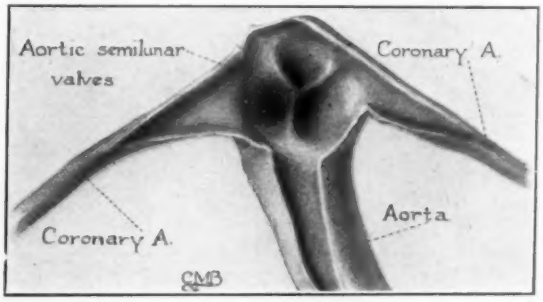

Fig. 6.—The opened aorta ascendens and two coronary arteries, showing the occluding septum which represents the fused semilunar cusps.

"cor pseudotriloculare biatriatum," as did Dolgopol[14] in reporting her similar specimen. This cavity measured 2 mm. or less in width, 7 mm. in depth, 19 mm. in height, and would contain probably less than 0.5 c.c. No opening into the aorta could be found.

The interventricular septum was strong and well developed. It corresponded to the interventricular sulcus, which was displaced far to the left (Fig. 1). At the extreme upper part of the pars membranacea septi there was a shallow depression with an interventricular patency. However, this aperture was so small that only a 2 mm. probe could be passed through it into the pulmonic conus region; when passed from the right side, the probe entered the left ventricle just below the occluding aortic septum described below. Even this tiny patency was closed by a small tag of the septal cusp of the tricuspid valve which was attached to the upper edge of the septum by a thin chorda tendinea.

Although the arch and ascending part of the aorta admitted a thin wire, it could not be passed beyond the aortic ring. When the vessel was opened (Fig. 6), a complete occlusion, i.e., atresia, of the aortic valve was found. This was due to a transverse septum (*X* in Fig. 3), showing on its upper surface three shallow excavations separated by three low ridges which extended from the center of the septum 1.5 to 2 mm. along the aortic wall (Fig. 6). The septum represented the

fusion of the three semilunar cusps; the excavations, the sinuses of Valsalva; and the ridges, the lines of fusion of the cusps. The three little pits were of equal size, and corresponded in position to the normal cusps.

Arising from the right anterior and the left anterior excavations were the right and left coronary arteries. When opened, neither showed any union with the pulmonary artery or with any chamber of the heart. Their courses were normal in relation to the heart chambers.

Microscopic Examination.—Extreme thickening of endocardium, especially in left ventricle; atrophy of muscle fibers and replacement by dense fibrous connective tissue in left atrium and ventricle; congestion of vessels, especially near endocardium; no actual connections of vessels with the lumen of heart were found after detailed serial section study.

LITERATURE

The classical monographs on congenital heart disease dismiss aortic and mitral atresias with but a passing comment on their rarity and the associated extreme degree of morbus ceruleus. Many of the articles entitled "aortic atresia" are found to be descriptions not of real atresia but of stenosis of varying degrees. Aortic stenosis usually is not accompanied by the extreme cyanosis seen in atresia, nor is the prognosis so grave. In the following tabulation only those cases of true anatomical atresia are listed. A very careful search of the available literature and bibliographical aids revealed only fifteen cases of aortic atresia such as seen in this case. Some of these, however, differed in the associated cardiac anomalies.

Abbott[1] in her monumental collection of 850 cases of congenital heart disease found only six cases of aortic atresia.[2-7] In five of these there was an associated septal defect, and the foramen ovale and ductus arteriosus were nearly always widely patent. One of her cases was that reported by Summons[2]; his patient lived for fifteen weeks, which is by far the highest age attained by any reported case. Cyanosis and dyspnea were the prominent clinical features, as in all the cases.

Other instances apparently similar to the one here reported have been described by Philpott,[8] Bellet and Gouley,[9] Willer and Beck (two cases),[10] Farber and Hubbard,[11] and Wesson and Beaver.[12] Aortic atresia has been reported in two cases of cor biloculare (Hastings[13]; Konstantinowitsch[3]), in a case of transposition of aorta and pulmonary artery (Dolgopol[14]), and in three cases of cor triloculare biatriatum (Moore and Menne[4]; Dudzuz[5]; Shapiro[15]).

The case of Bellet and Gouley[9] is important because both the interatrial and interventricular septums were completely closed, and because of the "remarkable finding of numerous circular and oval channels in the left auricular appendage and left ventricle, some of which could be found by serial sections to communicate apparently with coronary arteries, through remains of the embryonic sinusoids. Thus it appeared that blood passed through them from the coronary arterioles to be delivered to the cavity of the left auricle and ventricle." [However, it

may be more likely that they served for passage of aerated blood from the left auricle and ventricle into the myocardium to aid in its nourishment.]

Farber and Hubbard[11] reached the conclusion that "fetal endomyocarditis was the cause of cardiac anomalies, especially in such cases as atresia or stenosis of valves." In fourteen collected cases of valvular stenosis or atresia (four being their own), they stated that "infection during fetal life seemed to be evident from gross and microscopic pathology." As in their instance of aortic atresia, in all these cases they found "enormous thickening of the endocardium (in the left ventricle), with hyaline degeneration in the muscle bundles, with abundance of finely divided fat droplets in the muscle fibers, and with definite calcification and cicatrization near the atresia." Three of their cases showing these changes were earlier reports of aortic atresia (Ruge[6]; Loeser[7]; Bellet and Gouley[9]).

Although partially descriptive, the titles of "truncus solitarius pulmonis" (Shapiro[15]) and "cor pseudotriloculare biatriatum" (Dolgopol[14]) are quite misleading.

DISCUSSION

The size of the foramen ovale, and consequently the amount of blood that might pass through it, apparently were factors influencing the duration of life. All cases in which the duration of life and the size of the foramen ovale were mentioned have been arranged in a sequence according to the length of life (Table I). It is evident that the larger the foramen ovale, the longer the infant lived.

TABLE I

CASE*	LENGTH OF LIFE	SIZE OF FORAMEN OVALE	
	HOURS	MM.	REMARKS
1. Bellet and Gouley	12	--	"Completely closed."
2. This case	20	3 × 2	"Guarded by flap."
3. Loeser	40	--	"Open."
4. Willer and Beck, Case 1	43	4 × 3	"Small."
5. Wesson and Beaver	60	6.0	"Guarded by flap."
6. Philpott	62	9.0	"Widely patent."
7. Willer and Beck, Case 2	96	7 × 4	"Patent."
8. Shapiro	96	7.0	"Absent interventricular septum."
9. Dolgopol	120	--	"Widely patent."
10. Hastings	144	--	"Absent interatrial and interventricular septa."
11. Moore and Menne	144	--	"Relatively large patency."
12. Summons	2,520	--	"Extremely wide patency."

*In Case 1, Farber and Hubbard,[11] the patient lived thirty-six hours, and the diagrams accompanying the protocol illustrate a foramen ovale patency of 4 to 6 mm., according to a personal communication from Dr. Farber.

The course of the blood was probably as follows (Fig. 3). Venous blood returning from the systemic circulation entered the right atrium. All of it passed into the right ventricle through the tricuspid orifice; its

entry into the left atrium was probably blocked by the flap guarding the foramen ovale. In the right atrium it was mixed with the small amount of aerated blood which could pass through the foramen ovale from left to right. From the right ventricle this mixed blood entered the pulmonary artery, then either the ductus arteriosus or the right or left pulmonary artery. Returned to the left atrium from the lungs, all or practically all the blood from this chamber reached the right atrium via the foramen ovale. Possibly a minute quantity of blood passed through the stenotic mitral orifice into the hypoplastic left ventricle, but having no outlet through the atretic aorta this would have been forced to return to the left atrium through the mitral valve. It is extremely doubtful that the minute interventricular patency would have admitted blood into the right ventricle, in view of its size and especially the presence of the guarding tag of the septal cusp mentioned above. Blood from the pulmonary artery entering the ductus arteriosus was continued into the descending thoracic aorta, or some of it might have entered the stenotic aortic arch in a retrograde direction, to be then distributed by its three branches, the innominate, left common carotid, and subclavian arteries.

Blood reached the coronary bed in the myocardium from one or more of the following sources: (1) From the ductus arteriosus, by passing through the arch of the aorta and down the stenosed ascending aorta to the coronary arteries; (2) from the lumen of the heart, through the Thebesian veins or the arterioluminal channels described by Wearn and his associates;[16] (3) from the lumen of the right atrium through the dilated coronary sinus and its tributaries, as suggested by the congested coronary veins; (4) from the extracardiac anastomoses described by Gross[17] and recently emphasized by Beck.[18] Probably the first source was most important.

The extreme cyanosis resulted from a combination of the "determining factors" of Lundsgaard and Van Slyke,[19] in the following order of importance: 1. The "alpha" factor (right-to-left shunt), for it is evident that very nearly all of the venous blood must have been shunted into the arterial stream through the large ductus arteriosus. 2. The "D" factor (increased reduction of oxygen in the tissue capillaries), produced by a retarded rate of flow as shown by the generalized passive congestion. 3. The "1" factor (lessened or retarded oxygenation in the alveoli of the lungs), due to the abnormal obstruction to the outflow of blood from the left atrium by the mitral and aortic closures and by the small foramen ovale, and resulting in the pulmonary congestion.

Theoretically, aortic atresia might be due either to a prenatal inflammatory condition which brought about adhesion of the valve cusps, or to an abnormal or arrested development at some critical stage of cardiac morphogenesis. This latter cause might be the evidence of hereditary deficiencies in germ cells or of a chemical, hydrodynamic, or pathological

condition in the environment interfering with normal development during the early weeks when the septums and heart were assuming form. In cases so arising there may be additional gross departures from normal, such as dextrocardia, large septal defects, transposition or persistent ostium atrioventriculare commune. In such cases,[3, 4, 5, 13, 14, 15] the aortic atresia would seem to be a secondary defect, possibly following an unequal division of the bulbus cordis by a displacement of the aortopulmonic septum; if so, the cusps would adhere to each other from contact and compression even in the complete absence of inflammation. Displacement of this septum might have been due to hydrodynamic abnormalities following initial displacement to the left of the atrial or ventricular septums, or to asymmetrical subdivision of the atrioventricular canal.

There is no conclusive evidence for the existence of fetal endomyocarditis due to intrauterine inflammatory conditions, except in syphilis. Histological examination was made, however, in eight[6-12] of the fifteen previously reported cases of aortic atresia and in the present case. In all nine, certain changes were found in the left ventricle (especially near the aortic ring) which suggested the effects of prenatal infection. These changes included: thickening of the endocardium, complete or partial obliteration of blood vessels, fibrous scars, overabundance of immature types of fibroblasts and fibers, general replacement of muscle fibers by dense fibrous connective tissue, atrophy of muscle fibers, hyaline or fatty degeneration of muscle fibers, and calcification or cicatrization near the atresia.

Of the other seven cases (in which microscopic study was not made), six[3, 4, 5, 13, 14, 15] showed associated grave anomalies suggesting that the cause was active very early in cardiogenesis, with the aortic atresia probably being a secondary defect. In the other case,[2] there were no data upon which to base either conclusion.

In no case was there evidence of syphilis; in cases in which a Wassermann test of baby or mother was mentioned (six cases), it was negative. Nine were males, three females; sex was not noted in four. Color was not stated in seven; seven were white and two negro. The ages of the mothers (given in six cases) averaged nineteen and one-half years; the oldest was twenty-four years. Two of the patients were twins.

SUMMARY

The case reported here is the tenth showing aortic atresia associated with the usual combination of defects (mitral stenosis, left ventricular hypoplasia, stenosis of ascending aorta and arch, patent foramen ovale, right ventricular and pulmonary artery dilatation and hypertrophy, enlarged ductus arteriosus, and nonpatent interventricular septum). Six additional cases in the literature show grave congenital defects (absent

septums; transposition of aorta) associated with aortic atresia, making this the sixteenth recorded case of congenital aortic valvular atresia.

The probable course of the blood is suggested, especially for the coronary circulation.

All cases which have been studied histologically indicate that there might possibly have been a prenatal inflammatory condition; the alternate theory of arrested development is also discussed.

The size of the interatrial aperture or foramen ovale is shown to be a factor probably influencing the duration of life in cases of congenital aortic atresia.

It is a pleasure to acknowledge my appreciation to Dr. Harold Cummins, professor of microscopic anatomy, and to Dr. John H. Musser, professor of medicine, of the Tulane University, who read the manuscript.

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*Name often misspelled "Simmons."

SUDDEN ARTERIAL OCCLUSION IN THROMBOANGIITIS OBLITERANS*

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IT IS not surprising that occlusion of the main arteries may occur suddenly in thromboangiitis obliterans. In sclerosis of coronary arteries, which is a chronic occlusive arterial disease of a different type from that observed in thromboangiitis obliterans, sudden occlusion of the coronary arteries, which is recognized as thrombosis of the coronary arteries and myocardial infarction, occurs frequently. Sudden arterial occlusion in thromboangiitis obliterans has been emphasized in the monograph of Buerger, in the monograph of Brown, Allen, and Mahorner, and by Barker. Brown, Allen, and Mahorner said that "sudden arterial occlusion is usually indicated by sharp pain in the foot. Inspection shows extreme pallor and coldness of the extremity. Pain subsides gradually and usually disappears in from twenty-four to seventy-two hours. The pallor partially disappears and in the ends of the toes is replaced by excessive rubor or cyanosis. Claudication and other symptoms of thromboangiitis obliterans may follow shortly or be delayed for months. So frequently is this syndrome present that we make a tentative diagnosis of thromboangiitis obliterans in all cases of sudden unexplained occlusion of the peripheral arteries occurring in young adult males." Of sudden arterial occlusion, as an initial symptom, they said that "occasionally the first symptoms in thromboangiitis obliterans are those due to sudden arterial occlusion, consisting of the sudden onset of pain followed by pallor and coldness of the extremities. Some color and warmth usually return after prolonged rest, but mild pain on rest and claudication are the usual sequelae."

It is the purpose of this study to determine how frequently sudden arterial occlusion occurs in thromboangiitis obliterans, both as an initial event and as an episode in the course of well established thromboangiitis obliterans, to delineate the symptoms of this condition, and to study the events subsequent to it. For these purposes the records of 255 carefully studied cases of thromboangiitis obliterans were examined.

SUDDEN ARTERIAL OCCLUSION IN THE COURSE OF ESTABLISHED THROMBOANGIITIS OBLITERANS

This group consisted of fifteen cases, or about 6 per cent of all the cases which were studied. It is probable that the percentage incidence of sudden arterial occlusion in the course of thromboangiitis obliterans noted is low, as only characteristic incidences of this complication were

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included in the group. Were it possible to have a large number of patients with thromboangiitis obliterans under personal observation for a long time, it is probable that sudden arterial occlusion would be found to occur in somewhat more than 6 per cent of the cases. Sudden occlusion could be determined then, not only on the basis of symptoms, as was necessary in this study, but on the basis of sudden disappearance of pulsations in the peripheral arteries.

There can be no reasonable doubt regarding the diagnosis of thromboangiitis obliterans in any of these cases. All of the patients were men, except the patient in Case 15, who was a woman. The early details of this case have been reported previously as Case 16, by Horton and Brown. Chronic occlusive arterial disease is clearly indicated in each instance by symptoms of this condition, such as intermittent claudication, and by previous examination in many instances. The patients were all young or middle-aged individuals at the time symptoms of vascular disease were first noted, with the exception of the patients in Cases 5, 7, and 14. In each of these cases there was predominant evidence of an inflammatory type of arterial lesion rather than a degenerative one, although arteriosclerosis as a basis for arterial occlusion could not be entirely excluded.

It is apparent from this study that the time which elapsed between the onset of the disease and the appearance of sudden arterial occlusion varied within wide boundaries. One patient had had evidence of thromboangiitis obliterans for sixteen years before there was rapid interference with the arterial circulation; another one had had intermittent claudication for only three months previously (Table I). Symptoms likewise varied widely, from a sudden decrease in surface temperature to severe pain. This observation agrees with that of McKechnie and Allen; namely, that symptoms of sudden arterial occlusion not associated with chronic occlusive arterial disease are characterized by severe pain in only about half of the cases; in the remaining 50 per cent of cases, numbness, tingling, and coldness were predominant symptoms. As McKechnie and Allen have stressed in their previous study, the diagnosis of sudden arterial occlusion is not dependent on the accepted classic symptom of sudden severe pain in an extremity.

Sudden occlusion of arteries in thromboangiitis obliterans appears to be a serious complication as in ten, 66 per cent, of the fifteen cases it was eventually necessary to amputate the limb in which sudden occlusion had occurred. This is an extremely high incidence of amputation in thromboangiitis obliterans of all types, and exceeds the incidence of this operation in arterial embolism and thrombosis, which are not associated with chronic occlusive arterial disease, as the study of McKechnie and Allen showed that amputation is necessary in only about half of such cases. The explanation for the high incidence of amputation seems to be that extremities in which the arterial blood supply is already greatly reduced

TABLE I

SUDDEN ARTERIAL OCCLUSION IN ESTABLISHED THROMBOANGIITIS OBLITERANS

CASE	AGE IN YR.	SYMPTOMS		TIME OF SUDDEN OCCLUSION*	RESULTS OF SUDDEN ARTERIAL OCCLUSION
		BEFORE SUDDEN OCCLUSION	OF SUDDEN OCCLUSION		
1	44	Claudication for five years	Sudden pain	Three years	Amputation†
2	29	Claudication for one and a half years. Phlebitis	Sudden numbness and coldness; partial paralysis	Seven months	Ischemic neuritis; amputation eight months after acute occlusion
3	57	Bilateral claudication of feet for sixteen years. Right second toe had been amputated	Coldness and pain	Eighteen days	Claudication in right calf; rest pain relieved by treatment
4	37	Claudication of right calf, and later amputation of right leg	Coldness and redness of toes	Three weeks	Temporary recovery; leg amputated later
5	54	Claudication for three months	Sudden severe pain, and pallor and numbness	Nine weeks	Amputation; claudication developed later and there was occlusion of arteries of remaining leg
6	37	Claudication for one year	Sudden sensation of numbness and "deadness"	Three years	Temporary recovery; eventual amputation
7	51	Claudication for two years	Severe pain and coldness; numbness and partial paralysis	Three days	Amputation in one month
8	38	Claudication for ten years. Superficial phlebitis	Sudden discoloration and coldness of left foot	Eight months	Temporary recovery; amputation eight months after sudden occlusion
9	49	Claudication left arch and calf for two years	Sudden numbness and coldness of foot	Three weeks	Recovery from acute symptoms
10	44	Claudication. Amputation of left leg	Severe pain, cyanosis of toe nails, and anesthesia of distal half of foot	‡	Ischemic neuritis; gradual recovery; amputation in three months†
11	46	Claudication for one year	Sudden cramp in left foot	Three months	Recovery from acute symptoms in two days
12	28	Claudication for three years	Sudden onset of numbness, pallor and coldness of left leg	Three days	Residual ischemic neuritis which improved; amputation eighteen months later

*Before examination at the clinic.

†Elsewhere.

‡Sudden occlusion occurred while patient was under our care.

TABLE I—CONT'D

CASE	AGE IN YR.	SYMPTOMS		TIME OF SUDDEN OCCLUSION*	RESULTS OF SUDDEN ARTERIAL OCCLUSION
		BEFORE SUDDEN OCCLUSION	OF SUDDEN OCCLUSION		
13	35	Amputation of right leg	Numbness, coldness and discoloration of left foot	Three weeks	Recovery from acute symptoms
14	53	Claudication for two years	Pallor, coldness and pain affecting left foot and leg	Three days	Gangrene and amputation
15	30	Claudication	Sudden decrease in temperature of foot	‡	Recovery

cannot survive further sudden reduction in blood supply for long. It also is probable that cases in which sudden arterial occlusion occurs are representative of a more progressive form of thromboangiitis obliterans. Only two of these patients were under our observation at the time the blood supply to the extremity was suddenly diminished; the others were examined and treated at intervals ranging from three days to three years after the sudden thrombosis. Had all these patients received the very best of care immediately after thrombosis occurred suddenly, it is probable that amputation would not have been necessary so frequently. This, however, is by no means an absolute certainty.

SUDDEN ARTERIAL OCCLUSION AS AN INITIAL EVENT IN THROMBOANGIITIS OBLITERANS

There were eleven cases in this group, or about 4 per cent of the entire group studied. It is a fair assumption that the diagnosis of thromboangiitis obliterans is established when bilateral occlusive arterial disease of a progressive nature affects young men, when the onset of some of the occlusive lesions is gradual. In addition to bilateral arterial occlusion, no cardiac lesions were detectable which might be sources of embolism. Additional support for the diagnosis of thromboangiitis obliterans was the occurrence of superficial phlebitis in Cases 3 and 10, the gross and microscopic studies of the arteries in Cases 2 and 11, and the characteristic arteriogram in Case 9 (Table II). In all of the cases except Cases 9 and 10, the lesions affected the legs. All of the patients were men. In Cases 6 and 11 the occlusive lesion was unilateral at the time the patient first was examined at the clinic. In both cases, the diagnosis of thromboangiitis obliterans was made primarily, and subsequently was substantiated by the appearance of bilateral occlusion of arteries. In Case 11, the diagnosis was proved by microscopic examination of the arteries. Cases 2 and 11 were the only cases in which subsequent amputation was necessary. In Case 2 amputation was performed nine years after sudden arterial occlusion had occurred. In Case 11, the thrombo-

TABLE II

ONSET OF THROMBOANGIITIS OBLITERANS WITH SUDDEN ARTERIAL OCCLUSION

CASE	AGE IN YR.	SYMPTOMS		PROOF OF THROMBOANGIITIS OBLITERANS
		OF SUDDEN ARTERIAL OCCLUSION	SUBSEQUENT TO ACUTE OCCLUSION	
1	48	Sudden pain in left calf	None for one and a half years, claudication then appeared	Bilateral arterial occlusion
2*	39	Severe pain in right ankle and calf; leg pale; pain persisted two weeks	Claudication, ischemic neuritis, and gangrene after nine years; amputation	Bilateral amputation of legs; gross and microscopic examination of arteries
3	50	Sudden severe pain; numbness and immobility of right leg	Claudication	Phlebitis; bilateral arterial occlusion
4	45	Sudden pain in left calf and posterior thigh, and numbness of foot	Unknown	Bilateral arterial occlusion
5	39	Sudden severe pain in left leg, which lasted ten days	Claudication; gangrene of toes three years later	Bilateral arterial occlusion
6	42	Sudden pain in right calf	Claudication	Bilateral arterial occlusion†
7	36	Sudden numbness, coldness, and pallor of left leg	Claudication	Bilateral arterial occlusion
8	30	Numbness of left foot	Claudication	Bilateral arterial occlusion
9	37	Sudden numbness and coldness in left second finger, followed by ulceration	None	Claudication in legs two years later; arteriogram
10	39	Sudden pain and swelling of second, third, fourth, and fifth fingers of right hand	None after three months	Superficial phlebitis; bilateral arterial occlusion
11	40	Sudden severe pain in right midthigh; ten days later, same type pain in right calf; leg cold and white	Pain replaced by claudication in two weeks; ulceration of right great toe appeared three months later; amputation of right leg two months later	Bilateral occlusive arterial disease; microscopic examination of arteries
		Sudden severe pain, numbness and coldness of left leg, associated with disappearance of pulsations in femoral artery	Gangrene; amputation necessary	Microscopic examination of arteries; bilateral arterial occlusion†

*Patient had had symptoms in left leg and right hand five years before amputation of left leg, which was performed five years after onset of symptoms.

†At time of first examination arterial occlusion was unilateral.

angiitis was of a particularly malignant type, and it was necessary to amputate the left leg two weeks after sudden arterial occlusion had occurred, and it was necessary to amputate the right leg six months after the occurrence of sudden arterial occlusion. This patient was the only one of this group who was under our observation at the time of sudden thrombosis. The periods of known survival of limbs in cases in which amputation was not necessary following sudden occlusion of arteries were two and a half years (Case 1), six years (Case 3), fifteen days (Case 4), four years (Case 5), two years (Case 6), one year (Case 7), four years (Case 8), two years (Case 9), and twenty months (Case 10). It is apparent that the periods of survival of the affected limbs are considerably greater than those indicated, as many of these patients would have returned to the clinic for reexamination if further serious trouble had occurred. In Case 2 amputation was performed nine years after sudden occlusion had occurred, and this surgical procedure was hardly necessitated by sudden occlusion. In only one case (Case 11), or 9 per cent of Group 1, did the necessity for amputation eventuate soon after sudden arterial occlusion. When contrasted with the 66 per cent of amputations which eventually were necessary in the group of cases in which there was clinical evidence of thromboangiitis obliterans before sudden occlusion occurred, the number of amputations is remarkably small. The explanation seems obvious; when sudden arterial occlusion occurs in the presence of an already diminished blood supply, the consequences are much graver than when the arterial circulation is approximately normal. Intermittent claudication resulted in all cases except Cases 4, 9, 10, and 11. In Case 4 the information was not available. In Cases 9 and 10 the lesion affected the arms, and the second sudden occlusion in Case 11 resulted in gangrene, and amputation was necessary shortly afterward.

TREATMENT

Prompt recognition and treatment of sudden arterial thrombosis is important. It is probable that very little of value can be accomplished if twenty-four to forty-eight hours elapse before rational treatment is begun. Undoubtedly, other circumstances being equal, the prospects of a satisfactory recovery are proportional to the promptness with which logical treatment is instituted. Treatment of this complication is one which cannot be delegated judiciously to nurses or relatives, but warrants the almost constant attention of a physician until the circulation is reestablished, or until an unfortunate outcome is apparent.

There are three aims in the treatment of sudden arterial occlusion: (1) to relieve pain; (2) to avoid doing harm to the extremity, which has an impoverished blood supply; and (3) to induce as much vasodilatation as possible. Administration of morphine is advisable for the relief of pain. As in myocardial infarction, which is the result of thrombosis of a coronary artery, administration of large amounts of morphine may be

necessary, but the patient should be made comfortable. The placing of hot water bottles around the extremity is dangerous, as serious burns may result because the blood supply is greatly diminished and the tissues are very sensitive to temperatures which ordinarily are harmless. As a substitute for this time-honored method, we recommend wrapping the limb with absorbent cotton, which is held in place with an ordinary roller bandage. A cradle which contains electric light bulbs should be placed over the affected limb and covered with a sheet. The temperature within the cradle should not exceed 100° F., and a temperature of about 90° F., probably is advisable. The affected limb should be placed definitely below the level of the heart.

The outcome of sudden thrombosis of an important artery depends on the ability of arteries, which ordinarily are of secondary importance, to assume a heightened function of transmission of blood, that is, to undergo vasodilatation, since the occluded artery has become functionless by virtue of the thrombosis. The experimental work of Mulvihill and Harvey has demonstrated conclusively that the decrease in the circulation which follows arterial ligation can be offset completely by sympathectomy, which we assume either relieves actual spasm of collateral arteries or induces them to accept an increased function in contrast to that which they have normally. These observations are supported clinically by the encouraging report of Herrmann and Reid, who used an alternating positive and negative pressure (pavaex method) around the affected limb, and by the reports of Denk and of Allen and MacLean, who injected papaverine intravenously. Both of these therapeutic procedures produce a common effect, that is, arterial dilatation. In addition, vasodilatation can be effected in varying degrees by the oral administration of alcohol, as has been shown by Cook and Brown, or by the oral or intravenous administration of theobromine, as has been shown by Newell and Allen, and by Scupham or by the administration of acetyl-beta-methylcholine as has been shown by Goldsmith. Ethyl alcohol can be administered orally in orange juice or ginger ale, in doses of about 0.5 c.c. for each kilogram of body weight. The vasodilating effect of theobromine probably is too weak to be of use in sudden arterial occlusion, but the drug may be given by mouth in doses of 20 grains (1.3 gm.).[14, 17] Acetyl-beta-methylcholine should be administered by mouth in doses of 1 to 1.5 gm. We do not know the ideal dosage of papaverine hydrochloride; we have injected as much as 4 grains (0.24 gm.) subcutaneously and as much as 0.5 grain (0.032 gm.) intravenously in cases in which patients did not have vascular diseases, and these doses did not produce untoward effects of any importance. As a routine procedure it appears advisable to administer 0.25 grain (0.016 gm.) of papaverine hydrochloride intravenously, and to double this amount in thirty minutes if evidence of vasodilatation does not occur and if untoward effects are not noted. Injections can be repeated as needed if the first or second

one causes an increase in circulation to the extremity. At present our opinions regarding the efficacy of papaverine are *sub judice;* further observations are needed. If a machine, such as the ones constructed and described by Reid and Herrmann, by Landis and Gibbon, and by Krusen, is available, it should be used promptly, either alone or in combination with the vasodilating drugs indicated. Spinal anesthesia may be administered if the arteries of the legs are occluded and if the condition of the patient warrants it. Emmett has shown that maximal vasodilatation in the lower extremities follows this procedure. Theoretically, anesthetization of the brachial plexus should induce increased blood flow to the upper extremities. The artifical induction of fever by the intravenous injection of typhoid vaccine causes peripheral vasodilatation, as has been shown by Brown and others,[4] although its use in instances of sudden arterial occlusion is open to question because of the unpleasant side effects. Some of these unpleasant effects may be avoided by the artificial induction of fever by the intramuscular injection of sulphur in oil, which likewise produces vasodilatation, although pain at the site of injection may be severe.[20] Sympathectomy ordinarily is not indicated because it is a major surgical procedure and because the same results can be obtained temporarily with some of the methods which have been described.

Much that has been said about treatment is theoretical, but logical and true evaluation will depend on repeated clinical observation. Opportunities for this are rare as one seldom has the opportunity to treat a patient shortly after a main artery has been occluded suddenly. It may be well to theorize as to why prompt treatment is advisable. It has been known for a long time that the number of cases in which embolectomy is successful is inversely proportional to the time elapsing between the onset of embolism and the surgical procedure. The reason for this is not entirely clear, and it is not entirely clear why treatment must be prompt to be valuable in arterial thrombosis which occurs suddenly. It is certain, however, that failure to relieve spasm or to induce arterial dilatation, after either of these conditions occurs, leads to profound ischemia of the limb in most cases. If ischemia persists for several hours, it appears that the intima of both arteries and veins is so badly damaged that, when vasodilatation is accomplished, widespread vascular thrombosis occurs and ischemia becomes permanent instead of transient, as it would if vasodilatation had been induced soon after sudden arterial occlusion had occurred.

CONCLUSIONS

1. Arterial thrombosis may occur suddenly as a primary clinical manifestation of thromboangiitis obliterans. This situation occurred in 11 of our series of 255 cases, or, roughly, in 4 per cent. None of the patients were under our observation at the time occlusion occurred. Amputation was eventually necessary in two cases (18 per cent).

2. Arterial thrombosis may occur suddenly in the course of well-developed thromboangiitis obliterans. This situation occurred in fifteen, or 6 per cent of our series of 255 cases. Only two of the patients were under our observation at the time occlusion occurred. Amputation of a leg was subsequently necessary in 10 cases (66 per cent).

3. Treatment, which should be begun promptly, consists of relief of pain, avoidance of burning the limb, and the relief of arterial spasm, or the induction of vasodilatation, by means of drugs, intermittent negative and positive pressure, artificially induced fever, or anesthesia.

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Department of Clinical Reports

METASTATIC CARCINOMA OF THE HEART

A Case Presenting Auricular Flutter, Symptoms of Coronary Thrombosis, and Congestive Heart Failure*

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CARCINOMA of the heart is usually metastatic, and in most cases the symptoms due to the primary process, or other metastases, are so conspicuous in the clinical course of the patient that it proves difficult, even in retrospect, to ascertain the part played by the involvement of the heart. The case reported here is one of bronchogenic carcinoma in which symptoms and signs produced by the metastasis to the heart dominated the clinical course. The case provided an interesting diagnostic problem inasmuch as a hemorrhagic pericarditis due to malignancy of the pericardium appeared to be the cause of symptoms suggesting both an acute surgical condition of the abdomen and acute coronary thrombosis. It is also noteworthy for several other characteristics that are among the less common findings in metastatic carcinoma of the heart.

CASE REPORT

History.—The patient, P. S., was admitted to Sea View Hospital, April 4, 1934. He was a white male, German by birth, aged forty-nine years. He was a chauffeur. His family history was negative. His past history was also essentially negative. He did not drink or smoke. He had been in good health and had maintained his body weight.

The duration of the history from the beginning of any symptoms or signs of illness until death was approximately nine months, and this can be divided into four periods: (1) A period of five months in which the chief symptoms were those of peptic ulcer (from November, 1933, to April, 1934). (2) A period of 11 weeks in which there was vomiting of small quantities of blood from time to time (from March 4, 1934, to May 25, 1934). (3) A period of six days in which coughing with hemoptysis occurred (from May 25, 1934, to May 31, 1934). (4) The cardiac period (symptoms resembling coronary thrombosis, an attack of auricular flutter, congestive heart failure) lasting thirteen days (from Aug. 15, 1934, to Aug. 28, 1934).

In the first period of five months he suffered pain in the left hypochondrium, recurring in episodes and relieved by food. A series of x-ray films of the gastrointestinal tract before he entered the hospital had established a diagnosis of peptic ulcer. He was refused operation for the peptic ulcer because of abnormal pulmonary signs suggesting tuberculosis, for which he was admitted to Sea View Hospital.

Physical Examination.—The patient was a well-developed, well-nourished adult male, showing no signs of acute illness. His weight upon admission was 139 pounds;

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it increased to 158, and again declined to 151 pounds. A general physical examination yielded essentially negative results, except for the signs in the thorax and abdomen. The lungs showed bronchovesicular breathing, with fine râles over the right upper lobe. The heart was moderately enlarged. The heart rate was 80 a minute. The rhythm was normal. The sounds were of normal quality. There were no murmurs. The blood pressure was 130/90. The abdomen showed slight tenderness in the right lower quadrant and in the epigastrium.

The urine showed a faint trace of albumin with occasional white blood cells and epithelial cells. The blood Wassermann reaction was negative. The blood count showed the following: Red blood cells, 4,470,000; hemoglobin, 80 per cent; polymorphonuclears, 61 per cent; lymphocytes, 28 per cent; monocytes, 7 per cent;

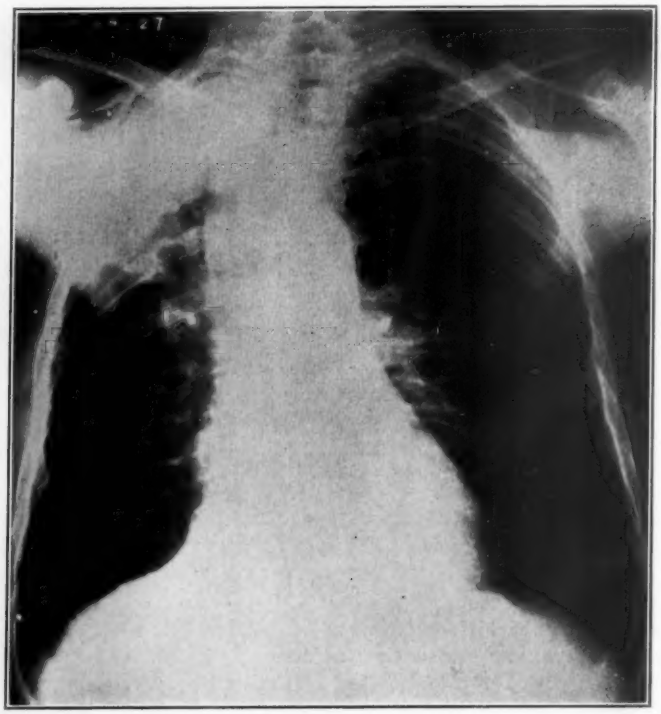

Fig. 1.—Roentgenogram taken April 16, 1934. Note lesion in right apex with displacement of trachea and mediastinum to the right; also essentially normal cardiac shadow.

nonsegmented polymorphonuclears, 1 per cent; eosinophiles, 2 per cent; basophiles. 1 per cent. The sedimentation rate of red blood cells was 47 mm. in forty-five minutes.

The x-ray examination of the gastrointestinal tract revealed an irregular filling of the cap and confirmed the diagnosis of peptic ulcer. The x-ray film of the thorax showed retraction and atelectasis of the right upper lobe with shifting of the trachea and mediastinum to the right (Fig. 1). This was interpreted as an end-stage of a caseous pneumonic tuberculous lesion. The results of repeated sputum examinations were negative for tubercle bacilli. The patient refused a bronchoscopic examination, and with the facts at hand the diagnosis of tuberculosis could not be established, nor the possibility of malignancy excluded.

Course.—His only complaints in the first seven weeks after his admission were those which were interpreted as due to the peptic ulcer, namely, pain in the epigastrium coming on an hour after meals and relieved by food, and from time to time vomiting of blood-tinged material. The patient received a Sippy diet and moderate improvement ensued. He then began to cough up small amounts of material with bright red blood intimately mixed with the sputum. This subsided after six days, following which he remained practically symptom-free for ten weeks (from May 31, 1934 to Aug. 15, 1934).

He was being considered for discharge from the hospital when the terminal episode started. There was a sudden severe attack of pain in the epigastrium with persistent vomiting for more than forty-eight hours. Two days following the onset, the patient looked extremely ill. The extremities were cold and clammy. The heart sounds were of poor quality and the rate very rapid. By the third day a friction rub was heard in the fourth intercostal space to the left of the sternum. An electrocardiogram showed a right axis deviation and auricular flutter with a 2:1 A-V block and a ventricular rate of 176 a minute. Marked rigidity was noted in the epigastrium and right upper abdominal quadrant. There was a rise of temperature to 100.4° F. The blood pressure throughout this period continued unchanged, namely, between 126/84 and 134/96. On the fourth day a sinus rhythm with a rate of 90 a minute had replaced the flutter. Diffuse signs appeared throughout both lungs—sibilant, sonorous, and fine moist râles. On the seventh day an area of localized swelling was seen on the right side of his neck due to a venous thrombosis. The electrocardiograms taken on the fifth and seventh days were similar and showed a sinus rhythm of 90 a minute, right axis deviation, and cove-plane T-waves in Leads I and II. There was no displacement of the R-T segments.

His condition became progressively worse. Heart failure with congestion developed; the liver became enlarged; edema appeared in the right side of the thorax and in the sacral region; and a right hydrothorax developed. The heart sounds grew barely audible. The temperature rose to 101° F. The white blood cell count rose to 17,850 with 83 per cent polymorphonuclears on Aug. 27, 1934. He died Aug. 28, 1934, thirteen days after the first appearance of symptoms referable to the heart.

The severe abdominal pain with vomiting, fever, and muscular rigidity, and the history of peptic ulcer, directed attention to a possible acute surgical condition of the abdomen. The signs of shock, the auricular flutter, the pericardial friction rub, suggested, on the other hand, a coronary thrombosis with symptoms referred to the right upper abdominal quadrant. This received some support from the electrocardiographic abnormalities seen when the normal sinus rhythm was reestablished. These and other diagnoses were entertained. The post-mortem examination failed to sustain them.

Autopsy.—The significant findings in the post-mortem examination were as follows:

1. A radial scar of a healed peptic ulcer was present in the duodenum just beyond the pylorus.

2. There was a right pleural effusion of 3,000 c.c. of pale yellow fluid.

3. A carcinoma involving the right main bronchus and the right upper lobe bronchus was found, with invasion of most of the right upper lobe. It invaded the right lower lobe posteriorly by lymphatic extension. The middle lobe was compressed but escaped metastasis.

4. There was no gross metastasis to the left lung, but in the microscopic examination small areas of tumor cells in the lymph spaces were found in the pleura of the left upper lobe. There was a thrombosis of a fairly large vessel in the midportion of the left upper lobe, with pulmonary infarction. The infarction may have been due to a primary pulmonary thrombosis or to an embolus from the venous thrombosis in the neck.

5. In the microscopic examination, the superior and inferior tracheobronchial nodes proved to be involved extensively.

6. There was a very dark, almost black, bloody, pericardial effusion of 300 c.c. Both layers of the pericardium were greatly thickened, especially the parietal, and their endothelial surfaces over all the chambers were studded with numerous indurated yellowish nodules about 1 to 2 mm. in diameter, covered by smooth, shining membrane (Fig. 2). The heart with the pericardium weighed 585 gm. and without the parietal pericardium, 250 gm. The appearance of the endocardium was normal. The aorta showed a few atheromatous plaques. Similar plaques were also present at the mouths of both coronary vessels but did not, however, reduce the size of

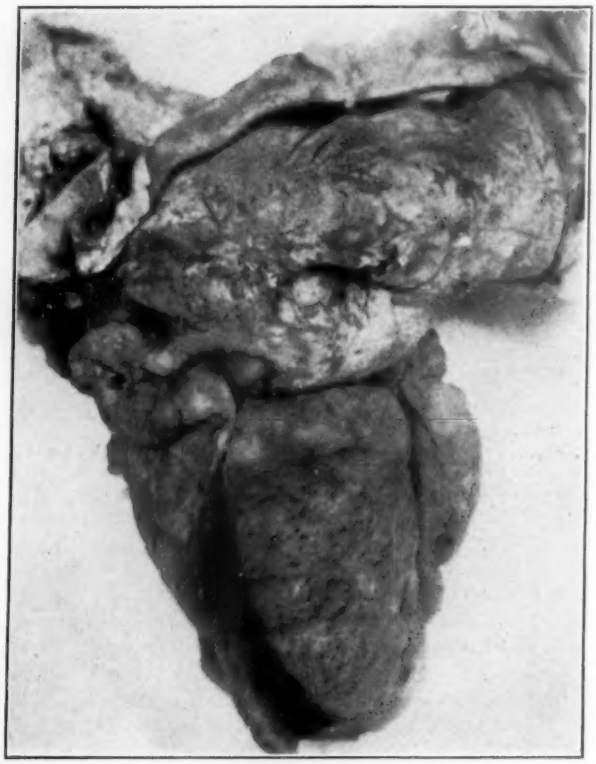

Fig. 2.—Post-mortem appearance of heart and pericardium. Note relative thickness of myocardium and pericardium.

the lumen appreciably. A careful search of the coronary vessels disclosed moderately advanced sclerosis of the arteries, but failed to reveal any thrombosis or areas of myocardial infarction.

7. The remainder of the complete pathological examination was substantially negative, except for those changes seen in congestive heart failure. The liver and spleen were moderately enlarged, the former weighing 1,890 gm., and the latter 125 gm.

The malignant tissue was squamous cell carcinoma. Fifty slides of tissue from the heart and the pericardium were examined, and in 11 several areas of sections from representative portions were inspected microscopically by each of three observers, who made independent estimates of the amount of malignant tissue in a

given area. The agreement between these estimates was usually very close and the averages were recorded. Malignant tissue was found to represent approximately 5 to 85 per cent of the cells seen in sections of the pericardium from various portions of the auricles and ventricles. In very few of the slides were malignant cells found in the myocardium. These areas were small, involving only about 5 per cent of the areas of the muscle examined, and, with only one exception, adjacent to the pericardium. In one slide of the interauricular septum about 60 per cent of the field represented malignant tissue.

COMMENT

The noteworthy characteristics of this case may be considered briefly as follows:

1. There was extensive invasion of the parietal and visceral pericardium, the myocardium remaining almost free from malignant tissue. The escape of the myocardium in cases in which both layers of the pericardium are extensively involved is an unusual finding. One such case was published by Campagna and Hauser.[1]

2. Since the tumor tissue in the pericardium was confined to the lymphatic spaces, there can be little doubt that the metastasis occurred through the lymph vessels. Except for those cases in which the heart is invaded by direct extension from massive thoracic malignancies, metastasis to the heart, in the majority of cases, is believed to take place through the blood stream.[2, 3]

3. The hemorrhagic pericardial effusion found at autopsy in this case is also an unusual finding in metastatic carcinoma of the heart. Usually metastatic carcinoma of the pericardium fails to produce an effusion of any kind.[1] However, when a hemorrhagic pericardial effusion is discovered during life, it provides fairly strong evidence of pericardial malignancy.[4]

4. Auricular flutter is also rare among the cases of carcinoma of the heart. Fishberg[5] recently reported three cases of auricular fibrillation and flutter in which tumor tissue infiltrated the auricular wall through to the endocardium. In our case the tumor tissue in the auricular muscle was confined to small groups of cells in the interauricular septum. The mechanism by which malignant tissue gives rise to auricular fibrillation or flutter is obscure. It seems likely that if a mechanical factor is responsible, it operates through interference with the circulation to the auricular musculature, since the abnormal rhythm may be paroxysmal (as in our case and in two of the three cases reported by Fishberg).

5. Thoracic pain is fairly common in patients with cardiac malignancy. It is usually impossible, however, to ascertain whether the pain is due to the involvement of the heart or of other mediastinal tissues. One of Fishberg's patients[5] suffered an attack of substernal pain attended by other symptoms which suggested coronary thrombosis. At autopsy, tumor tissue was found completely surrounding the circumflex branch of the left coronary artery, narrowing its lumen, and this was suggested as the possible cause of the attack of pain. In our patient,

the hemorrhagic pericarditis appears to be the most likely explanation of the sudden attack of pain with signs of circulatory collapse and auricular flutter, which had the clinical appearance of a coronary thrombosis or, because of the location of the pain, an acute surgical condition of the abdomen. The only other possible explanation found at autopsy is the infarct in the upper lobe of the left lung. This undoubtedly contributed to the fatal outcome but seems less likely as the primary cause of an attack of pain with muscular rigidity in the right upper abdominal quadrant.

An early reviewer of the subject of cardiac malignant disease[4] called attention to the surprisingly good functional capacity of the heart which is the seat of extensive invasion by malignant tissue. In our case, extensive involvement of the visceral and parietal pericardium covering all the chambers prevailed, without any appreciable cardiac insufficiency. Hamilton[6] reported a case in which the myocardium was almost completely replaced by malignant tissue, with relatively mild disturbance of the circulation. These serve to illustrate the large margin of safety in the heart muscle against gradually applied mechanical obstables, provided the muscle remains free of toxic influence. It presents a marked contrast to the rapidly failing heart in toxic states in which serious impairment of the functional capacity of the heart occurs, when relatively little gross structural change is in evidence.

The course of cancer of the heart is likely to be fairly rapidly fatal, however, after the beginning of symptoms referable to the heart. In our case, death occurred with congestive heart failure within thirteen days after the onset of cardiac symptoms.

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CARDIAC METASTASIS FROM CARCINOMA OF THYROID*

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CARCINOMA of the thyroid gland is not a rarity and is often diagnosed clinically before metastases occur. Occasionally distant metastases, especially in bone, focus attention on the thyroid as the primary source. Of such metastases, described in many organs, the rarest seem to be those to the heart. A careful review of the literature revealed but twelve cases. To these we add one which recently came under our observation.

REPORT OF CASE

On July 18, 1935, K. O., female, aged sixty-nine years was admitted to the Home for Incurables complaining of pain in the right hip and inability to move her right leg.

Family history was negative. Twenty-eight years before patient had had panhysterectomy for metrorrhagia and menorrhagia; three years before she had had an attack of cardiac decompensation.

One year before admission, onset of pain in the right hip, concomitant weakness, loss of weight, and belching after eating. One month later swelling and pain in the left ankle developed. Ten days before admission she felt her right leg snap at the hip without associated trauma and was unable to move her leg. No complaints referable to the thyroid; no swelling or lump was ever noticed by her.

Physical examination revealed a thyroid moderately enlarged to the right, somewhat firm; bronchial breathing in the right lower interscapular region with râles at both bases; right leg shortened, mobility preternatural at the right hip which was thicker than the left hip; swelling of the left ankle.

X-ray films showed fracture of right femoral neck with absorption of the outer half of the neck and all of the greater trochanter. Just above the left ankle joint the bones of both tibia and fibula were absorbed almost completely for almost one-fifth of the calf length. Bence-Jones protein was found in the urine. Blood count was 3,800,000, R.B.C.; hemoglobin, 60 per cent; 9,400, W.B.C.; lymphocytes, 35 per cent; eosinophiles, 3 per cent.

She became rapidly and progressively weaker, lost weight, and died two months after admission.

The clinical impression was metastatic malignancy, primary focus uncertain. Both gastrointestinal tract and thyroid were considered as primary foci.

Autopsy.—The thyroid was completely replaced by a firm mass in the right side of the neck and in midline, not compressing the trachea and easily separated from it. It measured 6 by 4 by 2 cm. and was covered by a capsule which was

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adherent to the surrounding fascia. On section a lobulated pinkish yellow homogeneous tissue bulged over the cut edge. There were small remnants of compressed beefy granular tissue containing calcific material at both upper and lower poles. Toward the right of the thyroid was found a large gland, 3 by 2 by 2 cm., its parenchyma completely replaced by tissue similar to that in the thyroid. Thyroid veins, jugular, subclavian, and innominate veins and superior vena cava were not grossly involved by tumor or thrombi.

The right pleural cavity contained 250 c.c. of a thin brown fluid and veil-like adhesions attached the lung to the anterior parietes and diaphragm. Both lungs presented a diminution of crepitation, edema, and a diffuse infiltration with small pink homogeneous nodules. The latter were prominent in the lower lobes and projected to the pleura. The right lower lobe was atelectatic and contained a great number of nodules.

The pericardial sac contained little serous fluid. The musculature was pale and flabby, and both ventricles were somewhat dilated. The right ventricular walls measured 0.4 cm. in thickness, and embedded in the right lateral wall, 3 cm. above the apex, was a spherical nodule. The nodule was of homogeneous pink color, measured 1 cm. in diameter, and reached to, but did not perforate, the endocardium. Thin musculature and epicardial fat bounded the nodule laterally. No other gross pathology was present.

There was no increase in peritoneal fluid. The liver presented accentuation of the central veins. On the upper right surface two small pink nodules projected through the peritoneal lining, one of which was umbilicated. Both nodules were soft and were surrounded by a narrow hemorrhagic zone.

In the lower pole of the right kidney a nodular mass occupied the parenchyma from the pelvis to, and causing bulging of, the capsule. The structure was similar to the other nodules except that radial striations were noted. Otherwise both kidneys were pale and unaltered. Uterus and adnexa were absent. The remaining abdominal organs merely showed cloudy swelling.

The head of the femur was freely movable from the neck and partially surrounded by a soft, slight, gritty pinkish white mass which replaced the neck, trochanter, and part of the upper shaft. Both marrow cavity and bone were replaced by this soft tissue mass 6 cm. thick and lined externally by a thickened continuation of the periosteum. The mass extended 8 cm. below the head of the femur, and the marrow cavity was red for 9 cm. below this level. The center of the growth was necrotic. The cortex immediately below the mass was sclerotic and widened to 0.6 cm. The left ankle presented a complete replacement by a similar growth in the lower fifth of the tibia and fibula.

Microscopic Examination.—The thyroid mass consisted of lobules separated by thick hyaline connective tissue. The lobules contained sheets of cells without arrangement, columns of cells with occasional irregular gland formation, and many groups of acini containing acidophilic cytoplasm and moderately hyperchromatic large oval nuclei. Occasional mitotic figures were demonstrable. Vascularity was pronounced and venules occasionally presented a partial lining by thyroid cells. An occasional plug of thyroid cells was found within the lumina of veins. No capsule was demonstrable, the glandular tissue invading the fibrous tissue in the neighborhood.

The lymph gland to the right of the thyroid was completely replaced by similar thyroid tissue, but the capsule was not invaded and the interlobular septums were thin. All the nodules grossly visible consisted of thyroid acini in more or less irregular formation containing colloid.

In the lower and middle lobe of the right lung, thyroid tissue occupied as much space as the lung parenchyma. The alveoli were atelectatic, forming by their parallel compressed arrangement poorly developed pseudocapsules for the thyroid growths, no fibrous tissue reaction occurring. The right upper lung contained several scattered nodules, the alveoli were emphysematous and contained albuminoid transudate.

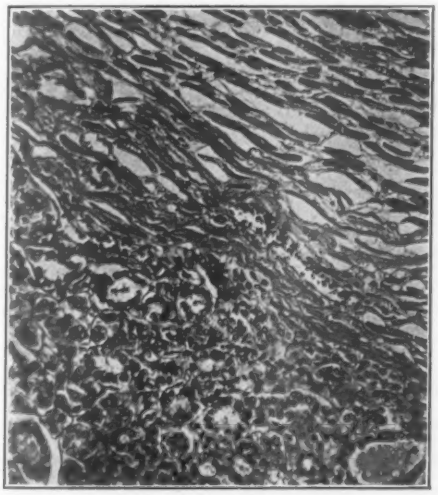

Fig. 1.—Photomicrograph of thyroid nodule in the myocardium. The atrophic heart muscle appears at the upper right.

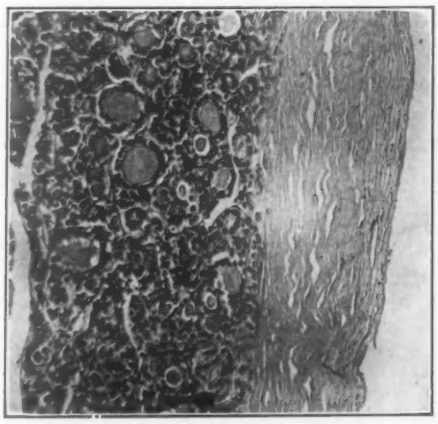

Fig. 2.—Photomicrograph of thyroid nodule in the subendocardial tissue. Note the thickened endocardium in the right midfield covering the metastatic tissue.

The left lung presented a similar picture, though not so pronounced. In both lungs the tiny nodules were demonstrable within the alveoli attached to alveolar septums in direct relation to the capillaries. Both lungs were intensely congested.

The heart muscle presented a slight patchy fibrosis and slight intimal thickening of the smaller coronary arteries. The nodule consisted of thyroid tissue with no lobular arrangement other than suggested by strands of hyalinized muscle fibers

caught in the growth. Acini infiltrated the surrounding muscle fibers, which were thinned and degenerated. The endocardium, though bulging, was thickened and not infiltrated.

The liver nodules consisted of thyroid acini, mostly small, without colloid. The surrounding liver cords were degenerated, compressed, and infiltrated by the glands. No fibrous tissue reaction had occurred. Otherwise the liver cells were hazy and granular.

The kidney parenchyma was compressed and infiltrated by the nodule of thyroid acini and cords of cells. Moderate fibrosis and round cell infiltration occupied the surrounding degenerating kidney substance. An occasional interlobar artery contained tumor emboli. The tubular epithelium was hazy and granular. An occasional interlobular artery presented intimal thickening, with narrowing of lumen and shrinking, even fibrosis, of the glomeruli. The spleen presented a hyperplastic splenitis. The adrenals and pancreas were unaltered.

The neck of the femur was occupied by thyroid tissue similar to that in the primary growth. Bits of bone were scattered in the mass, and larger necrotic areas were present deeper in the growth. The periosteal lining of the mass was thick, fibrous, and dense. The cortex adjacent to the growth consisted of dense, thick trabeculae of bone with relatively few cells. The medulla below the growth consisted of hyperplastic hematopoietic marrow, especially pronounced around neoplastic nodules. The left ankle presented a similar microscopic picture.

Diagnosis.—1. Adenocarcinoma of the thyroid infiltrating the surrounding tissue, metastasizing both by lymph and blood stream. 2. Right-sided serofibrinous pleurisy. 3. Right lower lobe atelectasis. 4. Cloudy swelling of parenchymatous organs.

The clinically relatively slight enlargement of the thyroid, and the absence of other evidence pointing toward the thyroid, were features. This, together with the gastrointestinal complaints and the presence of Bence-Jones protein, prevented the clinicians from arriving at a definite diagnosis.

Pathologically the main features were the relatively small primary growth, associated with numerous vascular metastases, the intense seeding of both lungs, the unusual myocardial metastasis, and the large growths in the lower extremities.

COMMENT

The study of metastases of carcinomas of the thyroid has occupied the attention of many authors in extensive reviews (Wegelin,[1] Barthel,[2] Ehrhardt,[3] Smith[4]). The conclusion generally reached is that invasion of the heart constitutes a rare finding, most reviewers having come across single cases in the literature.

Likewise carcinoma metastatic to the heart has been intensively reviewed (Goldstein,[5] Yater,[6] Morris,[7] Burke,[8] Ewing,[9] White[10]). In these reviews, though stating the possibility of primary source in any of the parenchymatous organs, the thyroid is not included in the enumeration. Metastatic carcinoma to the heart is so infrequent as to occasion interest and comment on its discovery. Nicholls[11] in 1927 reviewed 36,980 cases of carcinoma proved by autopsy. He found cardiac metastases in 109 cases, i.e., in 0.28 per cent of carcinoma.[11]

Nevertheless, a thorough search in the literature reveals a number of cases of cardiac invasion secondary to primary carcinoma of the thyroid, most of which are not listed by the reviewers.

Carcinomatous involvement of the heart from a primary neoplasm in the thyroid gland is of two types. In the first type, the right cardiac chambers are filled, to greater or lesser extent, by tumor thrombus reaching them by direct extension from the thyroid veins by way of the superior vena cava. This type more properly should be called neoplastic thrombosis rather than cardiac metastasis. In such instances the symptoms and signs are those of venous obstruction particularly in the head and neck, sudden dyspnea, and general venous stasis in the peripheral circulation. Death ensues in a manner similar to that in cases of massive pulmonary embolism. Of this type the following cases are recorded.

Kaufmann[12] described the case of a fifty-eight-year-old female with a goiter of twenty-eight years' duration. She suddenly developed difficulty in breathing and swallowing and edema and cyanosis of her face, upper extremities and chest; she died six months after the onset of the initial symptoms with the picture of acute obstruction of the pulmonary circulation. Autopsy disclosed a massive carcinomatous replacement of the thyroid. The neoplasm extended into the thyroid veins. Tumor thrombus filled the jugular and subclavian veins and the superior vena cava. The right auricle was completely filled with tumor thrombus; there was no invasion of the myocardium or endocardium. The cervical and mediastinal lymph nodes contained tumor; metastases were present in the lungs.

Holt's case[13] was that of a seventy-two-year-old male with known thyroid tumor of one year's duration. The thyroid mass had receded for two years following radiation therapy, but for a year there had been respiratory distress, slowly increasing cyanosis of the head, neck, and right arm, and edema of the legs. Attacks set in and rapidly increased in frequency and severity during the last three months, concomitantly the cyanosis becoming more intense. Death ensued in such an attack. Heart sounds, rate, and blood pressure were always normal. At autopsy the thyroid was found replaced by a firm tumor that extended into both innominate veins, filled the superior vena cava and right subclavian and internal jugular veins, and entered the right auricle. This cavity was filled with a polypoid tumor thrombus which was adherent to but did not infiltrate into the endocardium. There were no other metastases. Sections of thyroid and thrombotic mass were composed of adenocarcinoma.

Wylegschanin[14] reported the case of a fifty-two-year-old female who suddenly developed difficulty in breathing; a cough; a feeling of pres-

sure over the heart; edema of face, arms and abdomen; and cyanosis. There was a known thyroid enlargement of many years' duration. The heart sounds were muffled; the heart was not enlarged clinically. Death ensued one year from onset of respiratory distress and formation of mass in the neck. At autopsy, the lungs were markedly collapsed and congested, the lower lobes completely atelectatic; there was a large bilateral bloody pleural effusion. The pericardial sac contained 150 c.c. of clear fluid. The heart was enlarged by a marked dilatation of the right auricle and, to a lesser extent, of the right ventricle. This auricle was completely filled by a large tumor mass adherent to the posterior wall at the sino-auricular junction, but extending thence backward into and almost filling the superior vena cava, internal jugular and innominate and subclavian veins to the thyroid; even the vena azygos contained a thrombus. In the right ventricle a few small thrombi were loosely adherent to the endocardium between the trabeculae and behind the posterior tricuspid leaflet. The thyroid was converted into a dense, firm, gray white mass, sections of which, as well as sections of the thrombi, were composed of compact masses of irregularly cubical epithelium in places forming irregular and incomplete acini containing a little colloid. There were local lymph gland metastases and invasion into the sternothyroid and sternohyoid muscles; there was no extension into the endocardium and no pulmonary or distant visceral metastases.

Mencarelli[15] reported the case of a fifty-seven-year-old male who suddenly developed cyanosis and edema of the face and upper extremities. There were no cardiac symptoms or symptoms referable to the thyroid gland. Death ensued shortly after admission to the hospital, with the picture of acute edema of the lungs; total duration of symptoms from the onset was less than two months. At autopsy a large tumor was found replacing the thyroid gland and extending for some distance up and down the neck beyond the gland capsule. The right internal jugular vein was completely filled by a soft red yellow tumor thrombus. The innominate veins and superior vena cava were not grossly involved. The right auricle was dilated and hypertrophied. The right ventricle was filled by a tumor mass 6 by 4.5 cm., adherent to the anterior and posterior walls but not extending into them. There was only a small residue of ventricular lumen remaining on the anteromedial aspect between the interventricular wall and thrombus. The thrombus raised the tricuspid valve cusps so that they were in the position of closure and in contact. There were multiple tumor nodules in the lungs and one in the right kidney. All the viscera showed acute passive congestion. Histologically the thyroid tumor, venous and cardiac thrombi, and pulmonary and renal metastases were composed of masses of anaplastic and giant epithelial cells; a tendency to acinar arrangement was

present, but there was no colloid. No arteries, even to precapillary size, were invaded. The thyroidal venules were extensively invaded and filled with tumor thrombi.

The second type of cardiac involvement is truly metastatic in character. In this type the thyroidal veins may be invaded, but this is a microscopic finding. There is no dilatation of the cervical veins or the vena cava and no tumor or other thrombosis; nor do the cardiac chambers contain tumor thrombi. Metastatic foci are widespread throughout the body, involving especially the lungs and kidneys. In the heart the metastases are frequently deep within the ventricular musculature or, less frequently, the auricular musculature, but they may reach the endocardium. There is no recorded case of perforation through the endocardium, although there may be a reactive thrombo-endocarditis. In two instances foci were present in the interventricular septum.[19, 20] There is a longer interval between the initial symptoms and death. Attention is usually focused either on the thyroid tumor or, more often, on the bony metastases. Cardiac symptoms are lacking in the recorded cases; there is no record of electrocardiographic studies. Such dyspnea as is present is not associated with cyanosis or edema and seems to be due entirely to local pressure on the trachea or larynx. Of this type, of which our case is an example, the following cases are recorded:

Berard and Dumet's case[16] occurred in a fifty-eight-year-old male. No clinical history is appended. In the heart muscle were two nodules near the apex, the one in the right ventricle dipping deeply and extending to the endocardium, which was covered locally by a noncarcinomatous vegetation. In the left ventricular myocardium was a small subendocardial node. Metastases were present in the lungs, kidneys, and regional lymph nodes.

Van Straaten[17] reported a case in a fifty-five-year-old male with a seven-month history of enlargement of the neck, associated with pain locally and with ulceration (of the skin?). At autopsy metastases were recorded in the heart muscle, lungs, liver, and kidneys without further details. He further tabulated a series of thirty-five cases of carcinoma of the thyroid from Kundrat's Institute in Vienna, in which one case of myocardial metastasis occurred. No further details are given.

Ehrhardt[3] tabulated a series of 131 cases of carcinoma of the thyroid from Berne. Myocardial metastasis occurred once and pericardial metastasis once. No further details were recorded.

Thomsen[18] reported the case of a forty-year-old man with thyroid enlargement of four years' duration. Partial thyroidectomy was performed, the man living four and one-half years thereafter. Death was occasioned by the severe cachexia that developed. At autopsy there was found an adenocarcinoma involving the entire thyroid. There was pres-

sure on and invasion of the tracheal wall. The thyroidal veins were filled (microscopically) with tumor thrombi. In the left ulna, at the site of a previous injury, was a metastatic tumor growth the size of a child's head. Five pea-sized metastatic tumor nodules composed of thyroid carcinomatous alveoli surrounded by a fibrous capsular-like structure were found in the heart. Two were situated endocardially in the left ventricular apex between the trabeculae, one in a similar location in the right ventricle, and one deep in the left ventricular apical myocardium, also one in the right auricular endocardium. Numerous metastases were present in the skin; each was ulcerated.

Eisen's case[19] occurred in a fifty-two-year-old woman with dysphagia and a sense of a lump in the neck for two years. During the next year pains developed all over the body; a mass was found in the right breast, right hip, and right frontal region. A cord and mass slowly and progressively grew in the left cervical region and right axilla. The left eyeball progressively became more protuberant; a left primary optic atrophy developed. Death ensued two years after the onset of symptoms. At autopsy the thyroid was found replaced by an adenocarcinomatous tumor. Metastases were present in the lungs, liver, pancreas, kidneys, long bones and spinal column, right adrenal gland, left orbit, and the dura of the middle fossa. In the heart were several small polypoid nodular excrescences on the endocardium and between the pectinate muscles; these, composed of tissue similar to that of the thyroid tumor, involved the endocardium but did not invade the myocardium. One nodule, of unrecorded size, was found in the interventricular septum 2 cm. below the aortic leaflet. It lay between endocardium and myocardium and did not invade either structure.

Kopelowitsch[20] recorded the case of a fifty-two-year-old female with a known goiter of nine years' duration. Menopause occurred at fifty years, and about one and a half years thereafter there occurred a sudden, rapid diffuse growth of the goiter resulting in pressure on the trachea and esophagus. The heart was somewhat enlarged, the sounds were muffled, and a systolic murmur was present over the entire precordium, especially over sternum and aorta. Blood pressure and pulse rate were not altered. Biopsy disclosed a carcinoma of the thyroid. Death ensued two months after the onset of symptoms. Autopsy revealed a large adenocarcinoma of the thyroid with metastases to the cervical and bronchial lymph nodes, the lungs, and left kidney. In the heart there was a large tumor nodule in the right ventribular myocardium, extending from the coronary sulcus to the ventricular apex and bulging into the ventricle but not perforating the thickened endocardium. Two small nodules were present deep in the right posterior ventricular myocardium, and one in the midinterventricular septum. The pericardial sac contained a turbid red exudate; the epicardium was covered with fibrin showing no tumor histologically.

Wirth[21] reported the case of a forty-eight-year-old female who lived for one year following a thyroidectomy for a rapidly growing cervical mass causing choking, dyspnea, and dysphagia. At autopsy there was found an anaplastic carcinoma of the thyroid, infiltrating esophagus and trachea to the bifurcation. Metastases were present in the lungs and kidneys. In the right ventricular myocardium there was a nodule of acinar and anaplastic thyroid tissue, gray yellow and soft, wedge-shaped, extending through the entire thickness in its midportion but not penetrating endocardium or pericardium.

Cardiac metastases per se have not, in the past, exhibited any special symptoms. They may be suspected if attention is paid to the occasional pericardial hemorrhagic effusion. It may be that detailed fluoroscopic studies indicating disturbances of contraction locally, or electrocardiographic studies pointing to conduction disturbances, may point the way to such a diagnosis in instances of thyroidal neoplasm. In striking contrast to the usual type of metastases from thyroid carcinoma is the relative freedom of bony involvement in cases in which metastases occurred in the heart. Still more striking is the rarity of remote metastases in cases of thrombotic extension of a thyroid carcinoma by way of the great veins to the cardiac chambers. This suggests that death ensued, by vascular occlusion, before the secondary pulmonic foci had broken into their veins and gained access to the general circulation. A suggestive corollary is the frequency of pulmonic metastatic nodules in those cases showing true myocardial or endocardial metastases and remote organ involvement.

SUMMARY

A case of primary carcinoma of the thyroid with myocardial metastasis is reported.

Twelve cases of cardiac involvement from thyroidal carcinoma, reported in the literature, are reviewed. The clinical and pathological distinction between thrombotic extension into the cardiac chambers and true metastases to the myocardium and endocardium is stressed.

Attention is called to hemorrhagic pericardial effusion as a suggestive diagnostic point in cases of cardiac metastasis. Detailed fluoroscopy and electrocardiographic studies are urged as an aid in such diagnosis.

The authors desire to express their thanks to Dr. Henry Joachim, chief of service of the Jewish Sanatorium for Incurables, and to Dr. Thomas A. Gonzales, acting chief medical examiner of the City of New York, for permission to report this case.

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THROMBOSIS OF A CORONARY VENOUS SINUS IN A CASE OF THROMBOPHLEBITIS MIGRANS*

CASE REPORT

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NUMEROUS cases of wandering and recurrent thrombophlebitis, particularly of the superficial veins, have been reported, and several of them have been suspected, but not proved, to have had involvement of a coronary vein during the course of their illness. In the case described in this report, the clinical picture a short time before death led to a diagnosis of thrombosis of a coronary vein. At post-mortem examination the coronary sinus opening into the right auricle was found to contain a yellow fibrinous mass completely occluding its lumen. None of the other cardiac vessels were thrombosed.

Earlier writers[1, 2] on the subject of migrating or wandering phlebitis appear not to have observed any complications arising from thrombosis of visceral veins, and considered the disease as affecting the peripheral veins only. More recently, however, it has been shown by a number of observers that similar conditions of thrombophlebitis may occur in various organs of the body, and thus give rise to symptoms much more alarming than are associated with thrombosis of peripheral vessels.

Since the papers of Moorhead and Abrahamson,[3] who first called attention to the presence of visceral venous thromboses, and Ryle,[4] who considered four additional patients who had had similar accidents, a number of reports have appeared describing venous thromboses in various organs, including lungs, brain, intestines, and heart. The evidence of cardiac involvement has been based upon symptomatology and physical findings only. Thus, Legrand[5] reports a case in a woman who, during the course of her disease, had attacks of tachycardia. Moorhead and Abrahamson believed that severe anginal pain accompanied by a rapid, fibrillating pulse indicated thrombosis of a cardiac vein. Coombs[6] mentioned several cases in which phlebitis preceded the onset of what appeared to be a mild cardiac infarction and suggested that some such attacks may be "due to a venous thrombosis less disastrous in its mechanical effect on the circulation through the walls of the heart" than an arterial obstruction would be. Hartfall and Armitage[7] have described a case in which there occurred severe precordial pain accompanied by breathlessness and palpitation of such severity that morphia had to be used. They considered this to be a coronary thrombosis al-

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though the electrocardiogram was normal. Campbell and Morgan[8] have described a doubtful case in which there were definite electrocardiographic changes. In none of these did the disease end fatally, and the diagnosis of cardiac involvement could not be confirmed. Our case is of particular interest in this respect since post-mortem examination confirmed the clinical diagnosis of thrombosis of a coronary vein.

CASE REPORT

Mr. B. H., aged forty-five years, was admitted to the Medical Service, Toronto General Hospital, November 19, 1932, and died May 14, 1933.

The patient was first seen on Sept. 20, 1932, complaining of a tender red streak along the lower right forearm, which had appeared on Sept. 10, 1932. Subsequently, a similar condition developed on the left leg. Previous history of note was that for twenty years he had had chronic postnasal discharge for which several intranasal operations had been performed. In August, 1932, he had an infected tooth extracted, and, ten days before the onset of the phlebitis in his limbs, there was discharge from an apical abscess above another tooth. The examination at the time of his first consultation showed typical superficial phlebitis of right arm and leg. Rest in bed was advised. The superficial phlebitis continued and on November 12 he suddenly became short of breath, perspired, felt chilly, and began to cough, bringing up a small amount of bloody sputum. He was advised to come into the hospital.

On admission to hospital, he was quite ill: temperature 104° F., and pulse rate 100; he had some respiratory distress. Chest examination showed diminished resonance and some râles at the right base. Patient improved, the temperature fell to normal, and the signs in his chest had practically disappeared by December 6. Repeated white blood counts were between 9,000 and 10,000. During this acute illness the phlebitis of the superficial veins of both arms and legs continued. It was of a migratory type, jumping from one limb to another.

On Jan. 6, 1933, he again had severe paroxysms of coughing with frothy, clear sputum and pleural pain on his right side; the temperature rose to 101° F. A pleural effusion developed rapidly and on January 11 blood-tinged fluid was aspirated from the right pleural cavity. At this time the phlebitis, which had continued since November to involve the superficial veins of all four limbs in a flitting manner, affected the deep veins of the left leg, which became markedly swollen and painful. No definite foci of infection were found in teeth, upper respiratory passages, etc. On January 28, he again had pleural pain on the left side of his chest; a friction rub was heard; and his cough and shortness of breath, which were not constant, became worse. There was some evidence of consolidation, and the change in his left chest was considered to be due to pulmonary infarction.

Migrating phlebitis of the veins of the limbs continued, a new area becoming involved every few days. In addition, almost constant dyspnea developed, which was markedly aggravated by severe paroxysms of coughing producing a slight amount of whitish sputum. He became weaker, and his dyspnea and cough were much more troublesome. On March 1, 1,000 c.c. of blood-tinged fluid was removed from his left chest. It was considered that the respiratory symptoms were due chiefly to repeated thromboses of the pulmonary veins with resulting infarction.

Since September, when the patient came under observation, occasional extrasystoles were present, but on March 6 he became very short of breath and complained that his heart felt as if it was beating very rapidly. Paroxysmal tachy-

cardia was found, with a rate of 160. These attacks of tachycardia persisted at intervals until his death on May 14. At no time was there complaint of pain in the chest, which was thought to be cardiac in origin. There was no evidence of ascites, dependent edema, or enlargement of the liver. An electrocardiogram taken first on March 6, when he had his initial attack of paroxysmal tachycardia, showed rate of 170, with voltage 5 mm., with $T_{1, 2}$ positive. On March 9 the tachycardia had disappeared, with $T_{1, 2}$ definitely negative; one month later voltage still 5 mm. with $T_{1, 2}$ biphasic. The changes in $T_{1, 2}$ were not typical of coronary thrombosis and, probably, were digitalis effects, as he was given this drug after his first attack of tachycardia. The repeated attacks of paroxysmal tachycardia, the constant and increasing dyspnea, along with evidence of thrombophlebitis involving the superficial and deep veins of the arms and legs and the pulmonary vessels, led to a provisional diagnosis of coronary venous thrombosis. There was nothing absolutely diagnostic of this, but the signs and symptoms of coronary venous thrombosis may have been masked by the extensive process in the pulmonary vessels.

Dyspnea and paroxysms of coughing became more marked, and the course was progressively worse. On May 14 he became markedly short of breath and died.

The temperature records from September, 1932, to May, 1933, usually showed some degree of fever—up to 100° F. The fever rose to 101° and 102° F. temporarily after pulmonary thrombosis, with occasional rises with widespread peripheral thrombosis. It was impossible to state whether the coronary venous thrombosis produced fever.

Repeated white blood counts ranged about 9,000, reaching a maximum of 12,000 on two occasions, with a differential count of about 70 per cent polymorphonuclears. Blood chlorides, 470 mg. per cent; carbon dioxide combining power, 57 volumes per cent; calcium, 9.5 mg. per cent; phosphorus, 4.5 mg. per cent; bleeding time, 3 minutes; coagulation time, 3 minutes 45 seconds; platelet count, 184,000.

Seven blood cultures were taken, all of which failed to show any growth of organisms. Pleural fluid cultured on several occasions failed to show the presence of any organisms. A superficial vein with a very recent thrombophlebitis, and still showing a red streak on the skin, was surgically removed and culture of it by aerobic and anaerobic methods failed to show any organisms. In February and April, 1933, sections of veins were removed for culture and pathological study. The pathological report by Professor Oskar Klotz of the Department of Pathology was as follows:

"*Veins of Leg.*—This specimen of vein was received in February, 1933, when it was removed for bacteriological examination. The tissues proved to be sterile by the various procedures which were undertaken. The vein was a superficial one and was thrombosed at the time of its removal. The sections showed a thin-walled vein which in its surroundings was devoid of an inflammatory reaction but which contained a recent laminated red clot. The clot contained a fair number of leucocytes. The inner portion of the vein wall, including its intima and very narrow zone of the media, showed necrosis with a granular destruction of the tissue elements. There was no inflammatory reaction in this necrotic zone. In the remaining portion of the vessel wall no peculiar features were noted. One was rather struck by the absence of any reaction in the vein wall or in the tissues surrounding it.

"*Diagnosis.*—Phlebitis migrans with thrombosis.

"*Comment.*—The striking feature in this vessel is the absence of an adequate reaction which is usually considered necessary to play a part in thrombosis. In the vessel with the thrombus fully formed, the intima was found to show necrosis

of its elements without any inflammatory response. The thrombus itself was of the usual red, laminated variety, and no peculiar quality was evident in it. It would seem that the vessel wall is not the primary factor leading to thrombus formation. The question arises whether an altered state of the blood could account for the recurring thromboses."

At the time of death, the clinical diagnosis was thrombophlebitis migrans, the thrombosis affecting many of the superficial and deep veins of both arms and legs, the pulmonary veins, and involvement of a coronary vein.

A summary of the autopsy report from the Department of Pathology follows, and we are indebted to Professor Klotz for his particular interest in this case and for his personal opinion after examination of the sections.

AUTOPSY REPORT

Thorax.—The left thoracic cavity contained 1,000 c.c. of pinkish red, watery fluid, and there were a few fibrinous adhesions at the apex. The right thoracic cavity was almost entirely obliterated by fibrous adhesions but contained about 500 c.c. of similar fluid. The pericardial sac was adherent to the heart, and the wall of the sac was markedly thickened.

On the outer surface of the trachea there were a number of enlarged lymph glands: these were anthracotic and showed the presence of white, firm tissue, suggesting newgrowth. On opening the left main bronchus, it was found occluded by pedunculated, friable, papillomatous masses.

On cutting the lungs it was seen that the pulmonary artery had at various places firm white thrombi attached to its wall. There appeared to be no thrombi in the pulmonary vein. The cut surface of the lung was purplish red, with lobular distribution in scattered areas. The lung was firm and slightly raised above the surrounding tissues.

Heart.—The pericardium was attached to the heart by fibrous adhesions. The heart measured 12 by 10 by 4 cm. and weighed about 450 grams. The apex was blunt, and the surface was covered with a small amount of pericardial fat only. Both right and left ventricles were slightly dilated and hypertrophied. The coronary venous sinus, opening into the right auricle, was found to contain a yellow fibrinous mass completely occluding it. None of the remaining vessels of the heart were thrombosed. The myocardium was a good color and showed no evidence of vascular derangement nor fibrosis. Along the upper border of the left auricle and firmly attached to it was a considerable mass of newgrowth infiltrating the loose tissues about the heart and aorta. Some of this growth was present in enlarged lymph nodes. The right ventricle contained many round, white, firm masses. These masses consisted of small smooth-walled lumps of fibrin which had pedunculated attachments to the wall of the ventricle. Some of them lay between the neighboring musculi pectinati. Those attached by a pedicle were very easily dislodged from the point of attachment.

The wall of the left ventricle was free from these thrombotic masses and measured up to 1.5 cm. in thickness. The free border of the mitral valve was slightly thickened with white pinhead-sized nodular masses. The coronary arteries showed several small yellowish plaques in their lumina, but no stenosis was present.

Microscopic Report.—The microscopic report on coronary sinus, hypogastric vein, and heart was made by Professor Klotz. (Other veins studied in detail are not reported, but they were essentially the same as the ones described.)

Coronary Sinus: Sections were cut of the coronary sinus close to its mouth in the left auricle. At this point the sinus was completely occluded by a recent thrombus composed of a laminated clot. A considerable number of leucocytes were

collected in patches, while in other areas the clot appeared to consist of a granular material. Red blood cells had almost entirely disappeared from the clot. There was no evidence of organization.

Hypogastric Vein: This vein showed the presence of an old and a recent lesion. The old lesion consisted of an organized thrombus partially occluding the lumen, while the new lesion was that of a recent red thrombus completely obstructing the vein. The old lesion appeared to be in relation to the structures resembling valves. Numerous pigment-containing cells were seen in the tissues of organization where large numbers of capillaries were found. The adherent red clot showed early proliferation reaction on the part of cells near the surface of the intima, which were extending into the clot itself. As one studied the clotted mass within the lumen, the character of the thrombus suggested different ages to different portions. Parts could be picked out where the thrombus was progressing in the organization and the red blood cells were being destroyed. In other portions such changes were not encountered.

Heart: Sections of the myocardium showed normal-looking muscle fibers and an absence of an inflammatory exudate. There was no definite evidence of degenerative changes in the myocardial fibers although there was slight variation in the size of the individual elements. In one section taken near the endocardial surface a mixed thrombus was found lying within the mouth of a sinus. The deepest portion of this thrombus was attached to the wall of the sinus and was undergoing organization. Superimposed upon this was a more recent thrombus, rich in fibrin and containing many leucocytes. The musculature in the neighborhood of the sinus did not appear to be influenced by the presence of the thrombus. There was no degeneration of the muscle fibers.

Comment on Pathological Study.—In the various vessels which were examined, and these were all veins save for the pulmonary artery, thrombosing processes of varying ages were encountered. In many cases the vessel wall showed little reaction which could be associated with the presence of thrombus. In the pulmonary arteries, an acute reaction was found in the intima and media. These responses, as well as the hemorrhage about the artery, were often related to the presence of cancerous metastases within the lymphatic channels. This cancer arose in the bronchus. In the femoral artery, a chronic nodular phlebitis was encountered, but whether this had any relation to the thrombus is difficult to say.

It would appear from the autopsy findings and the histological study that the thrombosing process was the outcome of changes in the blood itself rather than the result of primary lesions in the vessel wall. The nature of such changes and the manner in which they were brought about is not clear. What part was played by the cancer of the bronchus and its extensions along the lymphatics of the lung is not possible to state, but our experience with a number of lung cancers does not suggest that these tumorous states have, in themselves, any peculiar effect upon the construction of the blood. Bacteria could not be discovered in the vessel walls by cultural methods, and the lesions encountered did not suggest a bacterial infection.

COMMENT

This case is of particular interest in that, during the course of the thrombophlebitis migrans, the sudden onset of paroxysmal tachycardia associated with dyspnea led us to make a provisional diagnosis of thrombosis of a coronary vein. At autopsy, complete blocking at the right coronary venous sinus by a thrombus was found. There was no apparent change in the heart muscle as a result of this thrombosis.

There did not appear to be any definite symptoms associated with coronary venous thrombosis. The clinical diagnosis was very speculative and depended on the presence of paroxysmal tachycardia in a patient with widespread thrombophlebitis migrans. The presence of multiple pulmonary artery thromboses and bronchogenic carcinoma may have masked the clinical syndrome of coronary venous thrombosis if there was one present. However, no precordial pain or distress was noted, and there were no electrocardiographic changes. It is obvious that there may have been other causes for the paroxysmal tachycardia, and it was not necessarily associated with the venous thrombosis.

The other point which arises from this case is that a thorough attempt was made to ascertain the cause of the thrombophlebitis migrans by clinical, bacteriological, and pathological study, and, as in many other cases reported, no etiological agent could be discovered. The suggestion of Smith[9] that multiple venous thrombi may be the result of latent malignancy is of interest in this case where bronchogenic carcinoma was discovered at autopsy. However, the incidence of thrombophlebitis migrans is not higher in cancerous patients than in noncancerous patients, and it is, therefore, impossible to state that the bronchogenic carcinoma was of etiological significance.

SUMMARY

A case of thrombophlebitis migrans is reported in which there was complete occlusion by thrombus formation of the right coronary sinus, as proved by autopsy. Thrombosis of a coronary vein was diagnosed clinically because of repeated attacks of paroxysmal tachycardia in a patient with widespread migratory phlebitis. No significant electrocardiographic changes were observed. At autopsy there were no changes observed in the myocardium that could be ascribed to coronary venous thrombosis. Careful study of the case by clinical, bacteriological and pathological means failed to show the etiological factor responsible for this case of migrating thrombophlebitis.

We are indebted to Professor Duncan Graham for permission to publish this case report.

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In Memoriam

GEORGE ELGIE BROWN

IN THE death of George Elgie Brown, at the age of fifty-one years, the medical profession has lost a real leader, just as he was approaching the pinnacle of achievement.

His dramatic rise from a general practitioner in the small community of Miles City, Montana (1911-1921), to chief of a section in the Division of Medicine of the Mayo Clinic, had all the elements of true romance and bore eloquent testimony to his exceptional qualities of mind and character.

His clinical research, which in the latter years was concerned chiefly with the field of the peripheral circulation, resulted in many outstanding contributions and his enthusiasm and energy were the sparks which activated many of the younger men throughout the country to carry on further studies in this field.

He was one of the small group which was responsible for the formation of the Section for the Study of the Peripheral Circulation of the American Heart Association and was elected the first chairman of the Section. To the great sorrow of its members, he did not live to preside at the first regular annual session.

Doctor Brown finely exemplified the glory of our guild, the desire to share not only with his close associates but with all humanity the best of his mind, his heart, his personality.

His untimely passing has been a crushing loss not only to his closer associates but to the multitude of his admirers and friends throughout the profession.

E. V. A.

Society Transactions

AMERICAN HEART ASSOCIATION, 1936

The twelfth annual scientific session of the American Heart Association was held on May 12, 1936, at the Hotel Phillips, Kansas City, Mo., with Dr. William J. Kerr as presiding officer. The following program was presented.

Program

The Coronary Flow in Hearts of Individuals Dying of Cardiac Insufficiency. William B. Kountz, M.D., St. Louis, Mo.

ABSTRACT

Revival of human hearts after death makes possible important functional studies. These are of more than usual interest when applied to the hearts of individuals dying of cardiac insufficiency and should throw light upon the nature of cardiac failure. Hearts of individuals dying of cardiac disease revive less readily than do hearts of individuals dying of other conditions than heart disease. Detailed studies could therefore not be made upon these hearts.

The total coronary flow of a normal heart whose weight was around 300 gm. was found to average, when perfused, about 812 c.c. per minute. The average flow per gram of heart muscle is about 2.7 c.c. per minute. In younger individuals the flow often exceeded this figure and sometimes equalled 5 c.c. per gram of heart muscle per minute. In the hearts of individuals dying of heart disease the total coronary flow may be greater than normal, especially in hearts where a marked hypertrophy had taken place, but when reduced to the terms of unit weight was found to fall below the level of 2 c.c. per gram of heart per minute. In subjects dying of heart failure the flow ranged from 0.75 c.c. to 1.5 c.c. per gram per minute.

These studies would lead one to believe that there is a danger in the reduction of coronary flow. This zone may be reached by hypertrophy and dilatation of the heart which appear to increase the need for blood, which, except perhaps in the early stages, is not supplied commensurately with the demand. In coronary arteriosclerosis the reduction may be due to disease of the blood vessels. In either case coronary artery inflow measured in terms of cubic centimeters per gram of heart is well below 2 c.c. per gram of heart muscle per minute.

The Pathologic-Anatomical Basis of Cardiac Insufficiency. Emmerich von Haam, M.D., New Orleans, La.

ABSTRACT

The frequently observed lack of striking morphological changes in failing hearts has always been a puzzle to clinical investigators, who have tried to explain the marked discrepancy between pathologic-anatomical and pathologic-physiological manifestations in heart failure with numerous terms such as acute myocardosis (Hyman) or essential myocardial insufficiency (Messinger). Little attention has been paid by most pathologists to the fact that accumulation of pathological changes cannot take place in a similar manner in the heart—the only organ of our body in constant active and rhythmic motion—as in other organs such as liver and kidney, and that cytological changes in the contracting heart muscle fiber will have a different appearance from similar changes in other cells. The necessary

consequence of such considerations, however, must be a different evaluation of morphological lesions in the heart with reference to organic function by a special system of cardiac pathology.

In attempting to investigate the pathologic-anatomical basis of cardiac insufficiency, material of 5,213 consecutive autopsies, performed during the years 1932 to 1935 at the Charity Hospital of New Orleans, has been studied by the author. During this period, 749 patients, or 14.4 per cent of the total number of autopsies, had died with the diagnosis of fatal organic heart disease. A comparison of the etiological and pathological types of heart disease in this series demonstrated hypertrophy as the principal factor in syphilitic, congenital, and hypertensive heart disease, degenerative lesions as the principal factor in toxic, pulmonary, and neurohormonal heart disease, and inflammatory lesions as the principal factor in infectious and rheumatic heart disease. The most consistent type of morphological changes in failing hearts was represented by the group of degenerative lesions associated with or superimposed upon cardiac hypertrophy.

The Relationship of Tachycardia to Cardiac Insufficiency. Drew Luten, M.D., St. Louis, Mo. See page 435.

The Dynamic Effect of Acute Experimental Poisoning of the Heart With Diphtheria Toxin. L. N. Katz, M.D., D. B. Witt, M.D., and E. Lindner, M.D., Chicago, Ill.

ABSTRACT

The acute effect upon the cardiac dynamics of injecting diphtheria toxin was studied in dogs. The study was based on records of mean arterial and venous blood pressure and records of the volume and pressure changes of the heart. Electrocardiograms were obtained also. The pressure curves of the various heart chambers (i.e., the two ventricles, the pulmonary artery, and the aorta) were recorded with Wiggers' manometer on a photokymograph. The volume and mean pressure curves were obtained on a smoked drum.

It was found that the diphtheria toxin, after preliminary acceleration, produced a sinus slowing of the heart, and later, various types of A-V and intraventricular block. Extrasystoles of various types and paroxysmal tachycardia also were present, and eventually the heart went into a peculiar type of ventricular fibrillation. A vasodilatation in both the systemic and the pulmonary circuits also resulted. Heart failure was caused by these disturbances in conduction and rhythm, and by the decreased coronary blood supply following systemic vasodilatation. There was definite evidence, however, that diphtheria toxin poisoned the heart in such a way that myocardial failure with its typical abbreviated and less powerful contraction occurred before these other changes came into operation. It is of practical importance to realize that diphtheria toxin acts directly on the contractile power of the heart since serious damage to the heart may be present without significant modification of the electrocardiogram or of blood pressure and heart rate.

Cardiac Asthma (Paroxysmal Dyspnea) and Failure of the Pulmonary Circulation. Soma Weiss, M.D., and George P. Robb, M.D., Boston, Mass.

ABSTRACT

Failure of the pulmonary circulation frequently develops independently of failure of the greater circulation. Cardiac asthma (paroxysmal dyspnea) results from acute and usually transient hypertension within the pulmonary circuit. The most frequent cause of attacks is acute or subacute left ventricular failure.

As indicated by clinical symptomatology, by circulatory measurements and by responses to chemical agents, there are three types of paroxysmal cardiac dyspnea which may occur singly or combined: (1) simple paroxysmal dyspnea without evi-

dence of bronchial spasm or intra-alveolar edema; (2) paroxysmal dyspnea with bronchial spasm and true asthmatic breathing; (3) paroxysmal dyspnea with intra-alveolar edema.

As judged from histological examination of the lungs, fatal paroxysmal cardiac dyspnea may occur without an appreciable degree of intra-alveolar edema, but with pericapillary edema. In this type of edema the tissue fluid is localized mainly between the capillary and alveolar basement membranes, but does not penetrate the alveolar basement membrane or the epithelial layer of cells. Hence the alveolar space contains no fluid. Such lungs may be heavy. In instances in which paroxysmal cardiac dyspnea is associated with true asthmatic breathing, there is sensitivity to histamine, and clinical improvement follows the administration of epinephrine. There are also instances of paroxysmal dyspnea regularly associated with diffuse intra-alveolar edema. This type is likely to occur in patients with advanced ("tight") mitral stenosis and in patients with arterial hypertension and uremia in whom osmotic pressure of the serum is low. Recognition of these types of pulmonary reaction in paroxysmal cardiac dyspnea bears on the therapy of this condition.

Cardiac Insufficiency in Coronary Thrombosis. Arthur M. Master, M.D., Simon Dack, M.D., and Harry L. Jaffe, M.D., New York, N. Y.

ABSTRACT

The rôle of cardiac insufficiency and related factors in the course and prognosis of 140 attacks of coronary thrombosis was studied. Congestive heart failure was more frequent in the older age groups and in those with a previous occlusion, hypertension, or enlarged heart. It developed in two-thirds of the cases and was usually combined left and right, although the lesion primarily involves the left ventricle alone.

The heart failure was classified as left or right on the basis of clinical signs and symptoms, venous pressure, circulation times and vital capacity. The latter proved a simple accurate measure of heart failure. The prognostic significance of tachycardia, low pulse pressure, poor heart sounds, gallop rhythm, tachypnea, orthopnea, pulmonary edema, cyanosis, fever, leucocytosis, hypertension, and cardiac enlargement was evaluated. Shock and congestive failure frequently occurred simultaneously.

Arrhythmias, though they tended to aggravate shock and heart failure, were transitory and required no specific treatment.

Heart failure increased the mortality rate. It was present in all but two of the thirty fatal cases and occurred equally in anterior or posterior infarction and in left or right coronary occlusion; more than one vessel was nearly always occluded; an old thrombosis was present in the majority, and the left coronary artery was usually initially involved.

The Differential Diagnosis of Congestive Heart Failure and Constrictive Pericarditis (Pick's Disease). Howard B. Sprague, M.D., Boston, Mass. See page 443.

Studies on the Effect of the Action of Digitalis on the Circulation in the Presence of Congestive Heart Failure. Harold J. Stewart, M.D., J. E. Deitrick, M.D., and N. F. Crane, M.D., New York, N. Y.

ABSTRACT

Studies of the effect of giving digitalis on the circulation have been made in patients exhibiting the signs and symptoms of congestive heart failure. Patients suffering from heart disease of rheumatic etiology, as well as those exhibiting

arteriosclerosis and hypertension, were included; in each etiological group there were patients exhibiting normal sinus rhythm as well as those in whom the rhythm was auricular fibrillation.

All observations were made with patients in a basal metabolic state. Observations were made first immediately before digitalis was given and later twenty-four hours after digitalis, 1.8 gm. (A.H.A. preparation), had been given by mouth, and then again at intervals later still. Records were made of the heart rate, of electrocardiograms, of arm-to-tongue circulation time (decholin), of venous pressure (direct methods), of cardiac output (acetylene method—3 sample technic), of size of heart (x-ray photographs of heart taken at a distance of 2 m.). In the patients who were observed, the giving of digitalis was associated with *decrease* in cardiac size, *decrease* in circulation time, *increase* in *cardiac output*, and *lowering* of venous pressure if it was elevated. The work of the heart before digitalis was given was not commensurate with the size, but following the administration of digitalis, the work accomplished at each beat became greater and more nearly commensurate with the size of the heart.

Inhibiting Thyroid Activity in the Treatment of Cardiac Insufficiency: A Report of Four Cases. James A. Lyon, M.D., and Edmund Horgan, M.D., Washington, D. C.

ABSTRACT

Four cases of cardiac insufficiency are reported in which improvement followed the devascularization of the thyroid gland to inhibit thyroid activity. In one case improvement has now been maintained for twenty-two months. This patient, who prior to operation worked with difficulty, is able to work regularly from ten to twelve hours a day without discomfort. His systolic blood pressure which formerly ranged from 150 to 300 mm. of mercury has now become stabilized at 140 mm. In another case improvement has been maintained for twelve months. This patient prior to operation was partially incapacitated for five months; since operation she has been able to work regularly for six to seven hours daily. Two patients have died. Both showed definite early improvement. One who had resumed work after having been incapacitated for three years prior to operation died of mesenteric thrombosis five months following operation. The other died of cardiac insufficiency twenty-two months following operation. With the exception of the last-mentioned patient, none has had a recurrence of cardiac insufficiency.

On the basis of the results obtained by the operation of devascularizing the thyroid gland to inhibit thyroid activity, the authors conclude that the method utilized by them has a place in the treatment of patients having cardiac insufficiency.

SECTION FOR THE STUDY OF PERIPHERAL CIRCULATION

Hemiconstriction of Vascular System Associated With Cerebral Disease. William J. Kerr, M.D., and F. J. Underwood, M.D., San Francisco, Calif. To appear in an early issue of this JOURNAL.

The Control of Sympathectomized Blood Vessels by Sympathomimetic Hormones and Its Relation to the Surgical Treatment of Raynaud's Disease. James C. White, M.D., Boston, Mass.

ABSTRACT

In line with the behavior of unstriated muscle in general, denervated smooth muscle in the arterial walls becomes abnormally sensitive to circulating sympathomimetic hormones as the vasoconstrictor nerves degenerate. The increase in sensitivity is much greater after degeneration of the postganglionic neurones than

after destruction of the preganglionic portion of the vasoconstrictor pathway. This has been measured in the rabbit's ear and the monkey's hand, as well as in human extremities. The most important hormone which mediates residual vasospasm in denervated arteries appears to be adrenalin. Sympathin and other, as yet unknown, substances probably play a contributory rôle. In explanation of the inferior results of cervicothoracic ganglionectomy, we have shown that this operation causes a degeneration of the postganglionic fibers to the brachial plexus, and thereby a maximal tendency to residual vasospasm during exposure to cold, exertion, or emotional stress. In contrast, lumbar ganglionectomy interrupts the vasoconstrictor outflow to the sciatic nerve in its preganglionic portion, and thereby leaves a minimal residual response to chemical stimuli. Application of these principles to the treatment of Raynaud's disease in the upper extremity is leading to a more physiological operation in which the ganglia giving rise to the postganglionic neurones are preserved, but the preganglionic connections are cut proximally. This method promises to give as favorable results in the arm as have been achieved in the leg.

Modified Dorsal Sympathectomy for Raynaud's Disease (Vascular Spasm) of the Upper Extremity. R. H. Smithwick, M.D., Boston, Mass.

ABSTRACT

In contrast to the excellent results which for years have been obtained from lumbar ganglionectomy for vascular spasm (Raynaud's disease) of the lower extremity, the results from a similar procedure; namely, cervicodorsal ganglionectomy, for Raynaud's disease of the upper extremity have been very unsatisfactory in our experience.

Extensive study of the anatomical and physiological considerations involved have led us to believe that it is possible to obtain satisfactory results in the upper extremity. A series of cases is presented in which a modified dorsal sympathectomy has been employed in order to sympathectomize the upper extremity. In this operation only preganglionic fibers are divided, and no ganglia are removed. A follow-up study of about twenty-five extremities over periods of a few weeks to over a year makes us feel that this operation will prove to be satisfactory.

One cannot speak too dogmatically about the results as yet until another year or so has passed. The chief cause of failure in the operation of ganglionectomy was probably due to sensitization of the blood vessels to circulating hormones, which cause residual vascular spasm after degeneration of postganglionic neurones. Adrenalin is probably the most important of the hormones in question.

If regeneration of nerve fibers does not take place, the operation should prove to be of considerable practical value.

Studies on the Nature of the Peripheral Resistance in Arterial Hypertension. Myron Prinzmetal, M.D., Los Angeles, Calif., Ben Friedman, M.D., New York, N. Y., Clifford Wilson, M.D., London, England.

ABSTRACT

Determinations of resting blood flow in the arm in various types of hypertension give an average value no greater than that obtained from subjects with normal blood pressure. This indicates that increased vascular resistance in the different types of hypertension is not confined to the splanchnic area but is generalized throughout the systemic circulation. Patients with hypertension show increase in blood flow in response to heat and reactive hyperemia equal in degree to that produced in normal individuals, showing that the blood vessels in hypertension are capable of considerable dilatation and indicating that the increased peripheral resistance is due to hypertonus and not to organic changes in the vessel walls. Sympathetic vasodilatation produced by the "heat test" produces no greater in-

crease in blood flow in subjects with high blood pressure than in normal individuals, suggesting that the vascular hypertonus is not vasomotor in origin. Patients with coarctation of the aorta, on the other hand, show a greater increase in blood flow in the arm in response to the heat test than do controls or patients with generalized hypertension. This demonstrates that vasoconstriction of sympathetic origin is present in the upper extremities in coarctation of the aorta and affords confirmatory indirect evidence that the hypertonus in generalized hypertension is not of vasomotor origin. Anesthetization with procaine hydrochloride of the vasomotor nerves to the arm produces the same increase in flow in normal subjects and patients with hypertension, proving that the vascular hypertonus is independent of the vasomotor nerves and that this hypertonus must therefore be regarded as intrinsic spasm of the blood vessels themselves. These conclusions apply to all types of hypertension, and hence there is no physiological evidence for the separation into "organic" and "functional" types or for the assumption that renal hypertension is due to vasomotor hypertonus. Surgical procedures aiming at the relief of high blood pressure by sympathectomy do not abolish the vascular hypertonus that is fundamentally responsible for the hypertension.

Anterior Nerve Root Section and Splanchnic Section in the Treatment of Hypertension. Irvine H. Page, M.D., New York, N. Y.

ABSTRACT

Since no treatment of medical nature is known which will lower arterial blood pressure more than temporarily in patients suffering from essential or malignant hypertension, surgical measures have seemed worthy of trial. The purpose of this investigation was to compare and ascertain the merits of anterior nerve root section and resection of the splanchnic nerves. (The operative procedures have been carried out by Dr. George Heuer at the New York Hospital.)

Favorable results have been considered marked and persistent lowering of blood pressure, regression of morbid eyeground changes, disappearance of subjective symptoms, and often decrease in the size of the heart. Our results may be grouped as follows as regards the outcome which may be expected from operation: (1) those patients in whom the disease is benign and in whom advanced vascular change has not occurred may respond well; (2) in those more advanced cases of long standing with morbid vascular change but benign in character, a favorable result may be obtained by no means certainly; (3) young patients, exhibiting hypertension bordering on the malignant variety and exhibiting symptoms and signs of the "diencephalic syndrome," may respond in a satisfactory manner; (4) patients suffering from highly malignant hypertension are far less likely to respond favorably.

In some of the cases relief has been dramatic; in others, especially those with highly malignant hypertension, operation has not appeared to influence the course of the disease. However, since two of five such cases were markedly benefited, operation may be worth a trial.

Nine patients have had supradiaphragmatic splanchnic resections performed. In all of the patients but two the disease was benign. Of the two, one was highly malignant and the other had marked reduction of renal efficiency. The results of this operation have been disappointing except in two of the very benign cases. Some reduction of pressure occurred in them, but it is too early (five months) to be certain that the pressure will not again rise. The remainder of the patients were not helped by operation.

A New Method for Determining the Circulation Time Throughout the Vascular System. Lester C. Spier, M.D., Irving S. Wright, M.D., and Leslie Saylor, M.D., New York, N. Y. To appear in an early issue of the JOURNAL.

Thorotrast Arteriography in Vascular Diseases of the Extremities, With Report of Illustrative and Unusual Cases. Wallace M. Yater, M.D., Washington, D. C. See page 383.

Sudden Arterial Occlusion in Thromboangiitis Obliterans. Walter F. Kvale, M.D., and Edgar V. Allen, M.D., Rochester, Minn. See page 458.

Ischemic Pain in Exercising Muscle: Its Nature and Implications. A. H. Elliot, Jr., M.D., and Richard D. Evans, M.D., Santa Barbara, Calif. To appear in an early issue of the JOURNAL.

Observations on Intermittent Claudication—Response to Treatment Measured Graphically. Lewis H. Hitzrot, M.D., Philadelphia, Pa.

ABSTRACT

The abnormal fatigue which occurs during contraction of the calf muscles deprived of adequate blood supply can be recorded graphically. In this study the variables due to voluntary control of the muscle contraction have been eliminated. The muscle group is stimulated electrically over fixed periods at varying frequency. A pen records the excursion of the foot extended with each stimulation; rest periods are so spaced to show recovery or lack of it after fatigue has been produced.

The presentation offers data from a study of the objective changes recorded by patients with suspected or proved vascular disease. Their fatigue curves show definite degrees of variance from normal standards which may aid in diagnosis and prognosis.

Comparison of the fatigue records of the same patient before and after treatment as with alternative suction and pressure or with injections of tissue extract, allow objective evaluation of such treatment. The fatigue curves have proved of value in cases in which the symptoms are equivocal or in which clinical evidence of progress under treatment is uncertain. Reproductions of individual and composite curves illustrate the clinical possibilities of the procedure.

DISCUSSION*

Discussion of the paper, "Coronary Flow in Hearts of Individuals Dying of Cardiac Insufficiency," by Dr. Kountz.

Dr. Fred Smith, Iowa City, Iowa.—Dr. Kountz has done some remarkable things with revived hearts. I doubt very much, however, if we are justified in drawing definite conclusions from the results reported. In the first place, the perfusion method is not a very satisfactory way of studying the coronary circulation in terms of absolute amounts. Moreover, we have no idea as to the extent of changes in metabolism which may have taken place in these hearts. The physiologists in recent years have demonstrated, among other things, that asphyxiation and reduction in the coronary circulation have a pronounced influence on the glycogen content of the myocardium. It is reasonable to assume that this must have a significant influence on the function of the heart.

Dr. Samuel Shelburne, Dallas, Texas.—I should like to ask Dr. Kountz if he has been able to make any observations during these experiments on oxygen utilization per gram of muscle weight, which might have some bearing on the things mentioned by Dr. Smith.

Dr. Kountz.—One certainly admits Dr. Smith's statements. These facts were made plain in the paper. The fact that one can revive hearts that have died, can

*The discussion of the papers presented before the Section for the Study of the Peripheral Circulation was not recorded.

make them beat, and carry normal blood pressures over periods of hours indicates that anoxemia and asphyxia probably do not play so much a part as one might suspect. Of course, in hearts of individuals dying of heart disease one deals with a somewhat different condition. These latter organs have been subjected to chronic asphyxia over a longer period, and chemical changes have occurred which are difficult to reverse.

Study of the coronary flow by oxygen utilization in these hearts has not been attempted. The method perhaps should serve as a check on our present work.

Discussion of the paper, "The Pathologic-Anatomical Basis of Cardiac Insufficiency," by Dr. von Haam.

Dr. L. L. Bresette, Kansas City, Mo.—How often do you find similar changes in hearts that do not present any clinical picture?

Dr. Simon Dack, New York, N. Y.—How often do you find no organic change in hearts which have failed?

Dr. von Haam.—In the study of 700 failing hearts I have never failed to find organic changes. The purpose of this study has not been to lay down strict rules of pathology concerning cardiac insufficiency but to demonstrate to you that all principal pathological lesions encountered elsewhere in the body during disease and associated with loss of organic function are also present in the failing heart. In order to correlate those morphological changes with loss of cardiac function resulting finally in cardiac failure and perhaps cardiac death, we have to use a different system of evaluation since the heart does not show accumulation of pathological changes in a degree similar to that found in other organs of the body.

Discussion of the paper, "The Relationship of Tachycardia to Cardiac Insufficiency," by Dr. Drew Luten, St. Louis, Mo.

Dr. L. N. Katz, Chicago, Ill.—Several questions are brought up by this interesting and challenging communication. A moment's reflection and an assay of the literature show that a fast heart is a much less efficient organ than a slow one. This is so for a number of reasons. In the first place, a fast heart has not as much time to recover as a slow one and is thus in a less rested state. In the second place, the heart is a poorer energy machine when it is beating rapidly than when it is beating slowly. In other words, it does less work for the same amount of energy.

In the third place, as Dr. Wiggers and I have shown, the distribution of the power of the heart is disadvantageously distributed in a rapid heart. To insist, therefore, that a rapid heart is a compensatory mechanism for the inadequacy of output gives a wrong impression of the efficacy of the circulation. It is generally conceded clinically that the prognosis is better for immediate relief of the failure when the heart is rapid than when it is slow. Obviously, this is so since when the heart is rapid, it can be slowed.

Furthermore, digitalis acts primarily to improve the efficiency of the heart. Dock has presented good evidence, some unpublished, which our work seems to confirm, that the action of digitalis may not be on the heart alone but on the venous return to the heart produced by narrowing of the venules, particularly those of the liver. Decreasing the amount of blood coming to the heart decreases its distention and so leads to the improvement. The action of digitalis on the heart is primarily on the conductivity of the impulse, particularly on the A-V node, and to a lesser extent on the irritability and responsiveness of the ventricles.

It is hazardous to dismiss the old point of view that tachycardia is a detrimental factor and substitute the view that it is a beneficial one. The converse is still the

opinion of most cardiologists. Thus, it is known that congestive failure may follow paroxysmal tachycardia in patients with organic heart disease.

Dr. Luten.—I hardly knew whether I was needlessly defending a point of view which has come generally to be held or offering something radically different. Dr. Katz has been kind enough to set me straight on that. The theory that the beneficial effect of digitalis lies wholly in its slowing effect is credited to Mackenzie, but Mackenzie was careful never to state that benefit is due entirely to slowing. It is true that any considerable degree of slowing occurs only in cases of fibrillation. That is the thing which attracts attention and which is easiest to measure; and the early conclusion was that improvement is due to slowing. Sir Thomas Lewis has insisted that reduction in rate is the only mechanism by which digitalis improves heart failure. You know better than that; you know that cases of heart failure improve after digitalis whether they have fibrillation or not, whether slowing occurs or not. You know that digitalis does have an effect on the heart muscle, whatever effect it may have on the conducting tissues.

I do not mean for a moment to deny that digitalis lessens conductivity. It is extremely difficult to prove it. If the auricle sends an impulse to the ventricle and one can measure the interval elapsing until ventricular response, I know of no proof that that interval represents only transmission time. I have no doubt, however, that digitalis does lessen conductivity. The point I am trying to make is that in view of the well-known effect of the drug on the muscle, we have centered attention too much on its action on the A-V tissues.

I did not have the time to refer you to work showing that in heart failure digitalis lessens ventricular irritability. It would appear only logical to assume (particularly with good physiological evidence) that impulses may reach the ventricle and not excite it. It is illogical not to take into account this lowering of ventricular irritability in heart failure as a prominent cause of the slowing.

If by its muscular action digitalis causes improvement in cases of heart failure with normal rhythm, will it not have the same beneficial effect on the ventricular muscle in the case of such a patient with an auricular circus movement? Must not at least a part of the improvement in patients with failure and fibrillation be due to the effect of the drug on the muscle, the same as in other patients wih failure? After demonstration of the fact that in congestive failure the muscular effect of digitalis is such as to cause improvement, why disregard entirely this well-known effect of the drug on the muscle and say that in cases with auricular circus movement the improvement is due to something else? Agents other than tachycardia are well recognized as causes of heart failure; relief need not depend on slowing.

One thing more: There is no obligation for one always to try to slow a tachycardia, whether it is associated with fibrillation or not. It becomes less and less a therapeutic objective. One used to try to induce slowing in a pneumonia patient with tachycardia. Attention now is directed elsewhere: if the patient improves, the rate declines. If a patient with heart failure gets better, his tachycardia subsides whether he has fibrillation or not.

Discussion of the paper, "The Dynamic Effect of Acute Experimental Poisoning of the Heart With Diphtheria Toxin," by Drs. Katz, Witt, and Lindner.

Dr A. R. Barnes, Rochester, Minn.—Mr. Chairman, I think we are greatly indebted to Dr. Katz and his coworkers for this excellent piece of work. I think he is right in diverting our attention from disturbances of conduction as a manifestation of diphtheritic infection of the heart. I thought Dr. Nathanson was here, and I hoped he would have a word to say because he has done some excellent work on this subject and he was one of the first men who called my attention to the fact that the T-wave changes were produced in the electrocardiogram in patients

sick with diphtheria independent of conduction disturbances. He amplified this work still further and reproduced the work experimentally in cats. He also pointed out to me the fact that in his experience the patients who had the T-wave changes in the course of their illness, even though they appeared to be getting along in excellent shape, not infrequently suddenly died and it became his custom when these T-wave changes appeared in the electrocardiogram to be unusually cautious in keeping these patients at bed rest for a long period of time. I think we ought not to neglect to give Dr. Nathanson the credit for having called our attention to this particular phenomenon.

Dr. M. H. Nathanson, Minneapolis, Minn.—I wish to point out that the results which Dr. Katz obtained in his experiments may not be applicable to clinical diphtheria. I do not believe that Dr. Katz intended to leave the impression that the acute poisoning which he produced necessarily represents the conditions which exist in the heart in diphtheria. I studied a group of diphtheria patients through convalescence and found marked electrocardiographic changes not uncommon, especially if the toxemia had been severe. These patients showed no signs of cardiac insufficiency. There may have been some disturbance in the dynamics of the heart, but this could not be detected clinically.

In clinical diphtheria the electrocardiographic modification may be, and usually is, the only indication that the myocardium is involved. An impairment in the contractile power of the myocardium sufficient to produce symptoms is rare, and when this occurs the electrocardiogram has already shown significant abnormalities. Death is usually sudden, without the development of symptoms and signs of decompensation.

Dr. Drew Luten, St. Louis, Mo.—Mr. Chairman, it occurred to me when Dr. Katz was reporting his extremely important work that it probably is another illustration of the viewpoint I tried to emphasize, that is, that the important thing is the effect on the whole muscle, rather than on such a small part of the muscle as the A-V bundle. His curve showed, if I followed him correctly, that there was evidence of ventricular impairment before conduction changes or rhythm changes were observed; and it struck me as a possibility, maybe a probability, that this very effect on the ventricle was the thing that produced the prolongation in A-V time, the muscle being involved, perhaps as much as the A-V tissues, in the exhibition of changes in the P-R interval.

Dr. William J. Kerr, San Francisco, Calif.—I would like to ask Dr. Katz a question. We know that the French use ouabain a good deal in patients following attacks of diphtheria, and I wonder if Dr. Katz has tried such substances on hearts studied to see what the result is in controlling the efficiency of the myocardium.

Dr. Katz.—In regard to myocardial changes, we have made some sections of these hearts, and the pathologist reports that there is nothing to see other than cloudy swelling, no hemorrhages, no evidence of necrosis. Our experiments were acute and not chronic, a fact which might not permit time for the development of morphological or histological effects. In chronic experiments, such as those of Dr. Nathanson, and in clinical cases, necrosis has been described. In other words, our effects were based on functional and not morphological effects.

I am grateful to both Dr. Barnes and Dr. Nathanson for their discussions, because I had no intent at all of ignoring the literature. Dr. Nathanson and I have discussed this problem several times, and I am well aware of his results. I think he is the first to have pointed out clearly that aside from conduction disturbances one should look for changes in the configuration of the ventricular complex.

I just want to rectify one statement that Dr. Nathanson made. We did not have evidence of congestive heart failure. We did find a rise in venous pressure on either

the right or left side. These are acute effects in animals and are important in that such acute effects may also occur suddenly in patients with diphtheria.

As regards Dr. Luten's discussion, there is no question that digitalis toxin and other poisons act on all the properties of the heart. The point is, which of the effects are dominant? Our results show that in spite of the slowing, the power of the heart goes down and not up.

We have had no experience with ouabain.

Discussion of the paper, "Cardiac Asthma (Paroxysmal Dyspnea) and Failure of the Pulmonary Circulation," by Drs. Weiss and Robb.

Dr. A. A. Getman, Syracuse, N. Y.—I should like to ask Dr. Weiss the reason for the paroxysmal character of the dyspnea. I understand quite fully, I think, why the patients have dyspnea, but I do not understand why it should occur in the evening, why we see it so often occurring at night, and why it is paroxysmal. Why do these patients not have dyspnea all the time?

Dr. Weiss.—If Dr. Kerr will permit me, I should like to answer that question in a little more detail. I purposely omitted that very important point because we had studied it previously and had already reported our experience.

I have tried to take up a few points bearing on the lungs only because I wished to emphasize that, in my opinion, the term "cardiac asthma" is a good one since it calls attention to the fact that there is not only a cardiac but also a pulmonary element. However, in cases of pure cardiac asthma, the heart is the primary trigger mechanism. It is in connection with this trigger mechanism that the question asked comes up, namely, "Why do attacks come on in paroxysms and why do they occur mainly at night?" First of all, they do not necessarily came on at night but may occur during the day, especially in advanced cases. On the other hand, it is true that a patient may be able to do his work in the daytime and then at night may develop serious attacks. We believe the reason for this is as follows: These patients, as I mentioned, have some pathology in the left ventricle which is just on the borderline of failure. Even if they are in a high pillowed position when they go to bed, very often during the night they gradually slide down. This lowered position of the lungs predisposes to pulmonary edema. We have actually observed patients whom we have placed in Gatch beds. After they were asleep, we have lowered the head of the bed and listened for pulmonary signs. At the base of the lungs we could hear râles develop. Then, while the patient is still in bed, for some reason the blood pressure becomes rather suddenly or gradually elevated. This may be brought about by a distended bladder, a desire to defecate, a night dream, or a great many other factors. Thus while the lungs are filling up, the arterial pressure suddenly becomes elevated. At this time the left side of the heart begins to fail and blood is trapped in the pulmonary circuit. The patient then wakes up, often with a feeling of distress or fright. This, of course, further increases the failure of the left ventricle. Failure may occur in the course of a few minutes, so that the pulmonary circuit becomes overfilled and distended.

The patient will get better in one of two ways: Improvement may occur spontaneously since, if the patient stays in bed, he may go into collapse or shock, producing a failure of the peripheral circulation which acts as a venesection. Thus, just when we think the patient's condition has become desperate, he begins to improve.

The second method of improvement is one commonly observed. The patient will tell you, "I have to rush to the window" or "I have to go to the bathroom to brush my teeth." Whatever bodily change causes the relief, it is always associated with an orthostatic position, although the patient does not know why he has a desire

to get up, to stand by the stairs, or to go to a window. As the patient stands, a certain amount of blood is pooled in the peripheral circulation and that relieves the pulmonary circulation.

Almost all the therapeutic measures which are successful in paroxysmal cardiac dyspnea are effective because they pool blood in the peripheral circulation from the pulmonary circulation, or because they overcome certain vasospastic reflexes, thus accomplishing the same thing.

In conclusion, in answer to this specific question, we believe that in cardiac asthma we are dealing with patients with borderline failure of the left ventricle. In addition, I wish to emphasize again that these patients have a reduced reserve of the pulmonary capillary bed. This capillary bed cannot distend; hence a small amount of blood trapped in the pulmonary circulation by the factors mentioned, either at night or during the day, will be enough to set up the sequence of events described.

Discussion of the paper, "Cardiac Insufficiency in Coronary Thrombosis," by Drs. Master, Dack, and Jaffe.

Dr. M. H. Nathanson, Minneapolis, Minn.—Dr. Master and his associates find a very high incidence of cardiac insufficiency associated with coronary thrombosis. I wish to point out that these figures are applicable only to the group which was studied, a group of hospitalized patients. If an analysis is made of a more general group, such as a series from a pathological department, the incidence of cardiac insufficiency is much lower, especially if the cases from the coroner's service are included. In an analysis of 113 autopsies of acute and chronic occlusive disease of the coronary arteries, I found that cardiac insufficiency as indicated by clinical symptoms and by passive congestion of the liver at autopsy, was present in but 42 per cent. In 58 per cent, death was sudden, and there was no evidence of cardiac insufficiency in the clinical history or in the autopsy findings.

I also found that cardiac insufficiency was far more frequent in coronary disease when the heart was enlarged. In 45 autopsies in which the heart weight was 400 gm. or less, cardiac insufficiency was present in only 7 per cent, while sudden death without cardiac insufficiency occurred in 93 per cent. In 68 autopsies in which the heart weight was above 400 gm. ranging from 450 to 600 gm., cardiac insufficiency was present in 63 per cent while sudden death without cardiac insufficiency occurred in 37 per cent.

Dr. Daniel J. Glomset, Des Moines, Iowa.—I want to make one comment on this interesting work; namely, that I do not believe it is possible to call any attack of coronary thrombosis or any attack of a myocardial infarct an initial one. From my own experience in dealing with somewhere around 100 of these cases, I believe there are a large number of these coronary infarcts which are asymptomatic, so much so that I presume that when symptoms are present, it is the second or third attack and not the first.

Dr. Howard B. Sprague, Boston, Mass.—I would like to point out in connection with this correlation between left ventricular failure and combined right and left ventricular failure, that, in coronary occlusion, we are dealing with a very diffuse involvement of the coronary circulation, involving both sides, and that the work which has just been done in our clinic by Dr. White and our associates has shown that next to mitral stenosis the most common cause of right ventricular failure is failure of the left ventricle. That is, after mitral stenosis, the greatest cause of enlargement of the right side of the heart is failure of the left. So that in the course of failure of the left ventricle in coronary occlusion involving the left ventricle, one would expect that the strain of this failure would be reflected very frequently in failure of the right ventricle, which often has also an inadequate coronary circulation due to the diffuse coronary sclerosis.

Dr. Fred M. Smith, Iowa City, Iowa.—I wish to stress the point raised by Dr. Nathanson; viz., that one is likely to get the wrong conception regarding the outlook in coronary occlusion from this paper. During the past few years a more optimistic viewpoint has developed concerning the prognosis of this condition. The analysis of any large series of coronary artery disease will disclose that a fairly high percentage have had a major coronary accident, and yet many of these will have recovered with quite satisfactory cardiac function even though the history oftentimes indicates that the patient is permitted to be up and about the next day or even a few days.

There have been relatively few instances of high grade cardiac failure during the acute stage of coronary occlusion at the University of Iowa. This perhaps may be due to the fact that our patients come from all parts of the state and many travel a considerable distance. Under these circumstances the more acutely ill patients are probably retained under the care of the family physician. Acute left ventricular failure is rather common immediately following cardiac infarction, but this is often a transient condition.

Dr. L. N. Katz, Chicago, Ill.—I am sure that Dr. Dack will assure us that these precise measurements were not needed to tell whether their patients had congestive failure or not. It is a bit hazardous routinely to subject patients with acute coronary thrombosis or occlusion with myocardial infarction to some of these tests. Further, it has been stated by a number of workers that the saccharin method and more particularly the ether method sometimes leads to serious complications. I would like Dr. Dack to report on their experience with this method. Have they had any fatalities and untoward reactions with these particular methods? These are not criticisms of the research, but simply made to prevent too much enthusiasm in using these methods routinely. There are only two laboratory methods which help the clinician routinely; one is the electrocardiogram, and the other is the sedimentation rate of the red blood cells.

Dr. A. R. Barnes, Rochester, Minn.—I should like to ask the essayist if he has any impression that involvement of the septum of the heart, particularly if it is extensive, played any predominant part in determining the occurrence of congestive failure. I am saying this because I have had a few experiences lately that lead me to suspect that infarction that involves the septum of the heart extensively has a much more important part in determining the occurrence of failure than an equal amount of infarction situated elsewhere in the heart.

Dr. Dack.—I would like to take up Dr. Smith's point first. We did not intend to paint a pessimistic picture of the outcome of coronary thrombosis. In fact, only recently we reported the results in a large series of cases. In more than 250 cases of coronary thrombosis the total mortality rate was only 16 per cent, which is much lower than the rates quoted in the literature. The mortality rate in the initial attack, as closely as we could determine, was only 8 per cent. We are thus not very pessimistic about the outcome of coronary thrombosis. All we tried to show was that when death did occur, cardiac failure was usually present.

In answer to Dr. Nathanson, we used ward patients because they could be subjected to much more accurate study. We included in this series all deaths, whether they occurred one minute or two months following admission. We have thus included all the sudden deaths in this series.

There were two sudden deaths among the thirty fatal cases, and these cases did not show cardiac insufficiency at clinical or post-mortem examination. One of these patients died of rupture of the left ventricle and the other of a convulsive seizure, cause unknown. All the other twenty-eight patients showed severe left and right cardiac insufficiency.

Concerning initial attacks, I think we were very careful in searching for a history of a previous attack. Of course, some closures are silent, and the presence of a previous thrombosis can be determined only at post-mortem examination. The majority of the hearts in the fatal cases show more than one closure.

Dr. Sprague's point about the cause of right ventricular failure is just the point that we tried to make. We never observed right ventricular failure alone; it usually followed left ventricular failure, and we think it was due to the severe strain put on the right ventricle following failure of the left.

We never observed a fatality following the determination of the saccharin or ether circulation time, although there have been one or two reports of fatal cases following the use of ether. However, in using saccharin one must not inject outside the vein, otherwise there is a very severe local reaction with much pain. We do not advocate these tests for routine use in diagnosis of cardiac insufficiency. We think that their main value lies in research study. We agree with Dr. Katz that most of our diagnoses could have been made without these tests.

One more point is that in most cases we can obtain as much information from the simple determination of the vital capacity as from the arm-to-tongue circulation time. In most cases it was a more delicate test of cardiac insufficiency than the other circulatory measurements. It was very valuable in following the course of a patient ill with coronary thrombosis. It is usually low after the closure, and, as the patient improves, it gradually rises. If the patient gets well, the vital capacity usually returns to normal.

Twenty-two of the thirty patients who died came to post-mortem examination. Of these, eleven showed gross infarction of the septum, whether the left or right coronary artery was occluded. All of these patients except one had signs of severe right ventricular failure in addition to left. The one exception died in pulmonary edema without signs of right ventricular failure. The eleven other patients, however, developed left and right ventricular failure even in the absence of septal infarction. Investigators like Fishberg think that when infarction of the septum occurs, right ventricular failure almost always follows. Libman has made the observation that signs of rapidly appearing right heart failure a few hours after a thrombosis indicate septal infarction.

Discussion of the paper, "The Differential Diagnosis of Congestive Heart Failure and Constrictive Pericarditis (Pick's Disease)," by Dr. Sprague.

Dr. William J. Kerr, San Francisco, Calif.—I should like to ask Dr. Sprague about the specific gravity of the fluid in the chest and in the abdomen in such cases. How often does he find a high specific gravity? And what significance does he attach to this finding?

Dr. Stewart R. Roberts, Atlanta, Ga.—This paper is well worth while. Constrictive pericarditis is so relatively rare when compared to the frequency of congestive failure that the former condition may not be even considered. In the South, due probably to the few cases of rheumatic fever compared with colder climates, it is a rare condition, though in the last year I have seen three cases. The third, fourth, and fifth ribs were resected in one of these cases, according to Brauer's operation as modified by Graham and done by Elkin. In the advanced degree of dyspnea, ascites, and little cardiac reserve, the two-stage operation may be wise and safer. Another patient lived to be seventy-four years old, but autopsy revealed the constriction and multiple external adhesions but no calcification. Another patient at the age of thirty-four years had the usual signs of constriction, concretio cordis, dyspnea, and pedal edema for eight years, marked systolic retraction of the epigas-

trium, and the anterior left interspaces, but no Broadbent's sign posteriorly. Pick's disease is not only often missed when it is present, but also it may be suspected when it is absent.

As Dr. Sprague stated, Broadbent's sign is often absent. Its absence is no proof that constriction is not present. Its presence is confirming and intimates need for proof of constriction. Excellence in cardiac diagnosis would discover constriction before early heart failure develops, much less proceeds to the degree of extreme congestive failure. When the diaphragm is tied by adhesions to the liver and spleen, and the liver is large, expiration ceases to be normal, and after years of varying degree of dyspnea, extreme emphysema may develop in the young as in the thirty-four-year-old man mentioned above. Retraction of the posterior interspaces may occur without epigastric pulsation or retraction, or epigastric retraction without the posterior interspaces moving. A dull ache arising in the precordial region and felt through to the left scapular region is suggestive. The diaphragm may be flattened bilaterally both by the emphysematous lungs above or by the adhesions below, or by both conditions. The firmness and largeness of the liver are suggestive of constrictive pericarditis. The lower border of the liver may reach to the iliac spine. The costophrenic angles may be filled with dense adhesions and misinterpreted as the fluid of a bilateral hydrothorax due to congestive failure alone. The pulsus paradoxicus should indicate the right cardiac diagnosis. Every case of congestive failure of doubtful etiology should include the technic of inspiration with the fingers on the radial artery. The absence of the apex beat or its independence of position and gravity intimates that more than ordinary congestive failure is present. Previous rheumatic infection with too early signs of early failure or congestive failure should raise the question of constricting adhesions.

A careful fluoroscopic study by the cardiologist himself is well. The heart that seems to beat by standing still at once raises the question. The amplitude of the systolic contraction may be a mere flicker in constriction. The wall of the poor ventricle is drawn out, but it cannot pull in as it would. The dense streaks and shadows of a concretio cordis may be apparent in the fluoroscopic study and be missed in the teleogram. When calcification is suspected, films taken with the further aid of the Buckey apparatus, and laterally as well as anteroposteriorly, may bring out far more clearly the proof and the degree of the calcification.

This is a difficult differential diagnosis to make. One would do well to maintain a mental attitude of care not to overlook a constricting pericarditis rather than the more dogmatic attitude of satisfaction that it is certainly not present. Not every patient with constricting pericarditis has congestive failure at the time of examination, and by far the majority of cases of congestive failure have no constricting adhesions, but the differentiation involves care in examination and equal care in interpretation and conclusion. Dr. Sprague, as usual, has read a good paper and rendered another service.

Dr. George Herrmann, Galveston, Texas.—Dr. Sprague has brought to our attention a very important group of cases and has contributed observations that are of inestimable value. I think, however, that the enthusiasm for surgical intervention should not be allowed to pass unchallenged or without a word of caution. I have had just a few experiences that have impressed upon me the necessity for caution. First of all, it must be admitted that for the most of us the diagnosis of constrictive pericarditis is difficult to make with certainty. Our experimental studies suggested new diagnostic methods which may now be realized with the kymographic study of movements of the heart and the electrocardiographic survey of Barnes. No diagnostic stone must be left unturned, we must insist upon adequate evidence for I know of two instances in which the pericardium was explored and found to be smooth and free throughout. Such mistakes we should not make, of course.

The other, an error of omission, is even more difficult to avoid. I refer to the recognition of the possible presence of a scar of the preceding myocardial infarction in a patient with adhesive pericarditis stenocardia. It is often a question of the interpretation of the symptoms. I believe that we might state that if there is a history of an acute pericardial process having been preceded or accompanied by severe pain, one should be cautious in making a diagnosis of acute pericarditis. One case in point was a young man who told of having had four years previously an acute attack of precordial pain which was accompanied by a friction rub and diagnosed as acute pericarditis. He had never recovered his usual exercise tolerance and careful study revealed clinical, roentgenographic and cardiographic evidences of adhesive pericarditis. He was scheduled for operation, but three days before operation, while on his usual afternoon ride in the country, he collapsed and died. At autopsy he presented adhesive pericarditis, it is true; but the pericardium formed most of the anterior wall of the heart, so that the decortication in his case would not have been a very successful procedure.

Another patient gave me a story of an attack of pain eight years previously along with a friction rub and symptoms of a very distressing type, with cyanosis and collapse which were considered to be the result of pericarditis with effusion. The case was followed very carefully by a physician, and recovery seemed complete until eight years later when symptoms of heart failure appeared. The failure was more of the type that has been described so well by Dr. Sprague as failure of constrictive type. His congestive failure cleared up, and we were ready to have him operated upon. Fortunately for us he developed acute bronchopneumonia and died. He had adhesive pericarditis, it is true, on both sides of the heart, but anteriorly he had an aneurysm of the pericardium. There was a hole about 1.5 cm. in diameter through his left ventricular wall, and it was completely healed at the borders and the blood had been passing through it out into the pericardium and flowing back again. Operative procedure in this case would have been a difficult matter also.

I believe therefore that caution is in order in the diagnosis of constrictive pericarditis before undertaking surgical treatment. We cannot be too careful in the study of such patients.

Dr. Harry A. Richter, Evanston, Ill.—How much fluid is necessary in acute pericardial effusion to make a diagnosis? Williamson and Willy in 1918 showed that small effusions tend to localize in higher levels at the base of the heart rather than at the apex.

I recently cared for a man with coronary occlusion who had a paradoxical pulse and other signs of pericardial effusion, which gradually increased in severity over a period of seven months, when death occurred. At autopsy a thrombosis was present in the left anterior descending coronary artery, and areas of infarction in the anterior wall near the apex, and 300 c.c. of clear fluid was present in the pericardial sac. The question came up as to whether or not the patient could have been helped by paracentesis.

Dr. A. R. Barnes, Rochester, Minn.—Mr. Chairman, I am afraid that Dr. Sprague has oversimplified this question of diagnosis. I have no doubt that in his hands it is easy, but I haven't found it so in my own. He did not stress the electrocardiographic findings.

I was sorry that Dr. Herrmann did not take the opportunity to discuss them a little, because he and his associates have written a most excellent paper on the subject.

We are at present engaged in an investigation of the electrocardiographic changes in pericarditis. I would like to call your attention to two or three electrocardiographic changes that have been of assistance in making a diagnosis of pericarditis.

In the first place, the electrocardiogram may record and reflect the fact that coronary occlusion is complicated by pericarditis. I pointed that out in a little publication, and the characteristic feature is the upward rounding and slight elevation of the RS-T segment in all leads. That type of tracing occurring in the presence of known occlusion indicates unmistakably, as far as I know, that that patient has a complicating pericarditis.

Now after having made that observation, I have had the opportunity to observe acute inflammatory pericarditis, and I have some excellent examples in which acute inflammatory pericarditis was indicated by this peculiar upward rounding and elevation of all RS-T segments and in one of which it was impossible by any of our methods of clinical examination to make the diagnosis which was proved at autopsy.

A few years ago Dr. Whitten and I had an occasion to study this, and we were struck with the fact that in adherent pericarditis there were an unusual number of tracings in which the T-wave was negative in all three leads. Dr. Sprague called attention to the fact that the T-wave may be negative in Leads I and II, and I quite agree with that and that the S-T segment may have a contour which resembles more or less closely that observed in an old healed myocardial infarction. The occurrence of negative T-waves in all three leads is a rather unusual electrocardiographic finding in general and that alone, or especially if coupled with low voltage in all leads, calls for careful exclusion of pericarditis.

Dr. Simon Dack, New York, N. Y.—I would like to ask Dr. Sprague how many of his cases of restricted pericarditis or calcified pericardium were subjected to surgery and what the results were.

Dr. James A. Lyon, Washington, D. C.—I should like to ask Dr. Sprague what the surgical management of these cases has been.

Dr. Sprague.—I am sorry, Dr. Kerr, that I am not able to give you statistical data on the specific gravity of the fluids from the abdominal and pleural cavities. There were seven cases with pleural effusions, a transudate in each case.

Dr. Herrmann has wisely cautioned us about surgical attack on these cases. I agree with him entirely that the story of pain at the beginning of an attack showing later pericarditis should make us very suspicious about the underlying pathology. The point about Pick's disease, however, is that one very infrequently sees the onset of the condition. If he does see the early stages, it generally appears to be fairly easy to make the diagnosis of acute, then subacute, then chronic pericardial inflammation, progressing very slowly over a matter of months, associated with fever and the evidence of fluid in the pericardium. I should not feel that in most cases of coronary occlusion the patients we see would be threatened with surgery and resection of the pericardium because in coronary occlusion and certainly in those cases which develop aneurysm of the ventricle the heart is badly damaged and is always enlarged. In the cases of Pick's disease that we operate on, the heart is small.

The question of how much fluid is necessary for the diagnosis of acute pericarditis from a practical point of view is not very important, because in acute cases one does not do anything about the pericardial effusion unless the signs of cardiac embarrassment arrive, that is, fall in blood pressure, increasing distention of the veins of the neck and enlargement of the liver. If there is not enough pericardial fluid to produce the picture, it is not necessary to go after it with a needle except for your own diagnostic satisfaction. If the diagnosis of fluid in the pericardium is very questionable, it seems hardly worth while to try to tap the pericardium.

I agree with Dr. Barnes and Dr. Herrmann that it is very difficult to diagnose these cases of Pick's disease. In the past seven years we have had intensive interest in our clinic through Dr. White's group and Dr. Churchill's group. Before that we

had the unfortunate experience, when the Brauer operation of thoracolysis was being done, of going in and finding the heart entirely free from pericardial adhesion, both to the chest wall and between the layers of the pericardium.

I wish to agree decidedly with Dr. Barnes on the subject of the electrocardiogram. I mentioned only the findings which we had in all the cases, and we have come automatically to consider pericarditis when we see the S-T and T-wave change in all three leads which he has mentioned.

At the present time fifteen patients have been operated on. Seven have been completely cured; one was partially relieved; three died primarily of the disease itself; three died of complications. There are two patients living in whom the diagnosis is not proved. Unfortunately there is not time to discuss the details of the surgical treatment.

Discussion of the paper, "Studies on the Effect of the Action of Digitalis on the Circulation in the Presence of Congestive Heart Failure," by Drs. Stewart, Deitrick, and Crane.

Dr. Drew Luten, St. Louis, Mo.—Mr. Chairman: In his summary I understood Dr. Stewart to say that digitalis has no consistent effect on cardiac output. I should like to ask him whether this statement was meant to apply to the effect of the drug generally, including both the normal and the dilated failing heart, or whether it is applicable specifically to cases of congestive failure. I appreciate the fact that in the normal heart the effect is to decrease output, but I got the impression from his paper that in his cases of heart failure Dr. Stewart found a rather consistent tendency for output to be increased. I should like to ask him whether his findings agree with Harrison's, which were that in the cases of patients with dilated failing hearts digitalis produces no consistent effect on the systolic discharge.

Dr. Stewart.—I purposely made the statement that the cardiac output *may* increase because this being a relatively small number of cases, one can conceive of a situation in which, such as in the case of the one patient with auricular fibrillation to whom we gave digitalis, the total cardiac output per minute did not change appreciably. His heart rate slowed from 80 to 50, and the heart became smaller. Now the work chart of that patient showed that the work of his heart was to his advantage at the slower rate and with the smaller heart, although from the cardiac output one might not have suspected that.

I have had occasion, both before Dr. Harrison published his observations and later, to go over his findings and point out certain similarities between some of his observations and some of ours. Maybe those in which he observed no change in cardiac output or a decrease in cardiac output were those in which the heart was made too small a pump. There are no observations of his relating to cardiac size, so it is not profitable to discuss this point further.

There is dissimilarity between the observations reported by Harrison and the observations which we are reporting in the manner in which the observations were made. All of our observations were made immediately before digitalis was given and then within twenty-four hours afterward because we were of the opinion that the early effects of digitalis were perhaps the important ones. Those of Harrison were made at variable times, both before and after the drug was given.

Discussion of the paper, "Inhibiting Thyroid Activity in the Treatment of Cardiac Insufficiency, A Report of Four Cases," by Drs. Lyon and Horgan.

Dr. William J. Kerr, San Francisco, Calif.—It seems to me Dr. Lyon has shown the right spirit to come before us and present some of the later effects or end-results in the limited number of cases of patients treated by this method. I wish that

some of those who were so enthusiastic about total thyroidectomy a few years ago would likewise come before us and tell us something about their end-results.

On the shores of the Pacific we are now beginning to see some of the patients who were operated on in the first flush of enthusiasm, and the results in those we have seen are far from encouraging. I recently saw a literary writer who was able to carry on and do some productive work even with a bad heart, but since thyroidectomy it has been impossible for her to stay awake long enough to finish a sentence, which does not make her a very facile writer.

Our own series of cardiac cripples upon whom thyroidectomy was done is small. We had one patient, however, with a marked aortic stenosis and severe pain of anginal type, where there has been almost entire relief of pain following a total thyroidectomy. This patient is a draftsman for a manufacturing concern, and formerly he could not work very much on account of pain. He had complete relief from pain, which makes life tolerable, but now he cannot work very much because he goes to sleep all the time. We are not able to find the level where he is able to keep awake, is free from pain, and can do any work.

This subject is open for discussion. We have not personally had any experience with the method which Dr. Lyon and Dr. Horgan have been using, but there probably are a good many who can say something about the section of the sympathetic fibers in these cases.

Dr. R. W. Langley, Los Angeles, Calif.—Some of us in Southern California agree with Dr. Kerr with regard to the value to be placed upon thyroidectomy as a procedure in controlling congestive heart failure. I think this very interesting paper leaves us more in a quandary than ever as to the rationale of this or any procedure which has to do with the interference of thyroid gland function and its relation to control of heart disease.

I would like to ask Dr. Lyon about the operative time required for this procedure compared with the time required for thyroidectomy and also about the amount of shock which these patients show following the operation.

Dr. Samuel Shelburne, Dallas, Texas.—Mr. Chairman, I don't see how there can be any way to evaluate the work that Dr. Lyon has done because I doubt if any of us have been able to observe patients with this ingenious procedure. I think it deserves a trial. However, it would be preferable to leave the trial in his hands for a good while, until we see how the results of total thyroidectomy are going to come out.

I have under observation at the present time a patient on whom we did a total thyroidectomy in March, 1934. He is a typical case of chronic coronary heart disease and was thrown into an attack of coronary thrombosis by an injection of insulin in December, 1933. He had been a subject of diabetes for about five or six years prior to that time.

This is a case history on a lantern slide. It is unusually satisfactory. First of all, I want to call attention to the change in blood sugar and discuss that briefly. Soon after the operation, this patient, who had moderately severe diabetes with blood sugar running up to 300, was to all intents and purposes cured of the diabetes by the total thyroidectomy. (You will notice it took about six weeks to have an effect from the operation on various bodily functions, basal metabolism and blood sugar.) I think in the future, if we may judge by the few cases that have had total thyroidectomy, diabetes is going to be affected profoundly by this procedure. But, as Dr. Kerr queried, is it worth while to cure the diabetes when the patient has to endure the unhappy symptoms of myxedema? This patient, of course, developed symptoms and signs of myxedema which were more disagreeable than those of diabetes. Several months after this operation, it became obvious to us we were either going to have a very, very unhappy patient or we were going to have to

put him on thyroid extract. You will observe that when enough thyroid was given to control the myxedema, the diabetes returned. I have been unable so far to find a happy medium.

Now, I have been interested for a good many years in the subject of edema, and I made some observations on edema in this patient. That is the point which I would like to pay most attention to at this time. The patient's edema was made worse by the operation. He developed one of the most extensive degrees of edema I have encountered in a fairly broad experience with these patients. It was so massive that I had to use needles to drain fluid from the subcutaneous tissue. Since Southey tubes were not available, we used Lindeman tubes which are just as good and, of course, cost much less. These were inserted under the skin of his legs, draining off large amounts of fluid. The edema was reduced. Thereafter we found that the usual diuretics were effective.

When the amount of thyroid, as shown in this chart by the depth of this black area here, was increased, this patient had less edema but he had a higher blood sugar and much sugar in the urine. It is obvious that this patient had less edema when he was on large doses (2 grains) of thyroid.

Dr. Blumgart, of Boston, advised me that a tenth of a grain or a fifth of a grain would be sufficient amount of thyroid to use. You see, in this instance, we cut down to about a fifth of a grain. During that period of low thyroid intake, his weight started right on up, and his edema returned. You see how frequently here we gave him mercupurin, a new diuretic which has proved very satisfactory to us. He does not have any sugar in his urine and his blood sugar is low. This will continue as long as we keep him on the low intakes of thyroid extract.

So, I would say that it is going to be a matter of time before we will be able to judge the effects of total thyroidectomy. This patient was one of the early cases, and he has been very closely observed. It seems to me that it is going to take a long time to find out whether we can strike a delicate balance between the various metabolic disturbances. There seems to be no question on the part of the men doing the work in Boston that this procedure is of great value in angina pectoris. This patient has had no pain since he had the operation. I sincerely doubt the value of the operation in the control of other symptoms and signs in heart disease or any great value in diabetes.

Dr. M. H. Nathanson, Minneapolis, Minn.—Dr. Kerr mentioned the physical and mental sluggishness and exhaustion of patients in whom a total thyroidectomy has been performed. I would like to suggest the use of a new substance, phenylisopropylamine (benzedrine), which appears to have a striking effect on these symptoms. Introduced recently by Prinzmetal and Bloomberg for the treatment of narcolepsy, I have found that there is a marked amelioration of such symptoms as fatigue, exhaustion, and drowsiness, which may be considered as mild narcoleptic manifestations.

I have not treated any patients following total thyroidectomy with benzedrine, but I have found striking improvement in the general condition of a group of patients with low metabolic rates who had little or no benefit from thyroid extract. The dose of benzedrine is small, 10 mg. once or twice a day. The peripheral sympathomimetic effects which might be very undesirable in cardiac patients, such as increase in cardiac output and the pressor action, are not produced by these small doses.

Dr. Howard B. Sprague, Boston, Mass.—I think perhaps I might be allowed to say one word since I come from the city where this procedure, complete thyroidectomy, originated. I merely wish to summarize the situation at present in Boston in this way by saying that at the Massachusetts General Hospital we have not performed any complete thyroidectomies for a considerable time, I think for a year; that at the other clinics in Boston, they are definitely in the stage of study-

ing the cases which have already been operated on and the enthusiasm for the procedure is definitely on the wane. Ever so often instances of quite remarkable relief after the procedure, whether related or not, are reported. The great difficulty is the one of selection of cases and no one that I know can tell before the operation what type of patient will be benefited. Dr. Lyon's procedure has the advantage of being a less serious operation and it appears that even after complete ablation of the gland the metabolism level does not correlate with the degree of clinical improvement. It may be that some other factor is involved, as Dr. Lyon's work suggests, and that his operation will give another series of cases which should be followed over a long period of time before the whole matter can be completely assessed.

Dr. Merritt B. Whitten, Dallas, Texas.—I would like to ask the essayist if any post-mortem study was made of the thyroid gland, in the cases that came to post-mortem examination, and if such a study was made, did it reveal any changes in the size or structure of the gland which might be considered a result of the operation?

Dr. Lyon.—The operation has been performed in 12 cases, 8 of angina pectoris and 4 of cardiac insufficiency. In the anginal group, 6 of the 8 patients have had no recurrence of angina pectoris for postoperative periods of from 5 to 28 months. One patient was not relieved of his attacks. There was one postoperative death.

Prior to operation the patients are kept at complete rest in bed for from two to eight weeks. In the cardiac insufficiency group, operation is not carried out until all signs and symptoms of congestive failure have disappeared. The patient is anesthetized by an inhalation of ethylene and a local infiltration of novocaine. A collar incision is used similar to that employed for a thyroidectomy. The operative time is about forty-five minutes.

We have made no biopsy or post-mortem study of thyroid tissue in this series of cases.

It is our opinion that metabolic readings are frequently not reliable indices of a patient's basal metabolism. This is especially true of patients who, because of aortic regurgitation, cardiac asthma, severe dyspnea, or extreme nervousness, are not able to cooperate in making the test. We, therefore, check the basal metabolic rate by the blood cholesterol level.

As to what constitutes improvement, we consider such changes in the patient's condition as the following:

1. A cessation, or a marked lessening in the frequency, of attacks of cardiac insufficiency.
2. A definite increase in the patient's ability to carry on regular employment without a return of symptoms of congestive failure.
3. A definite increase in the amount of exertion which the patient can undergo without discomfort, such as dyspnea, rapid heart action, or pain.
4. A lowering and stabilization of the patient's blood pressure or heart rate.